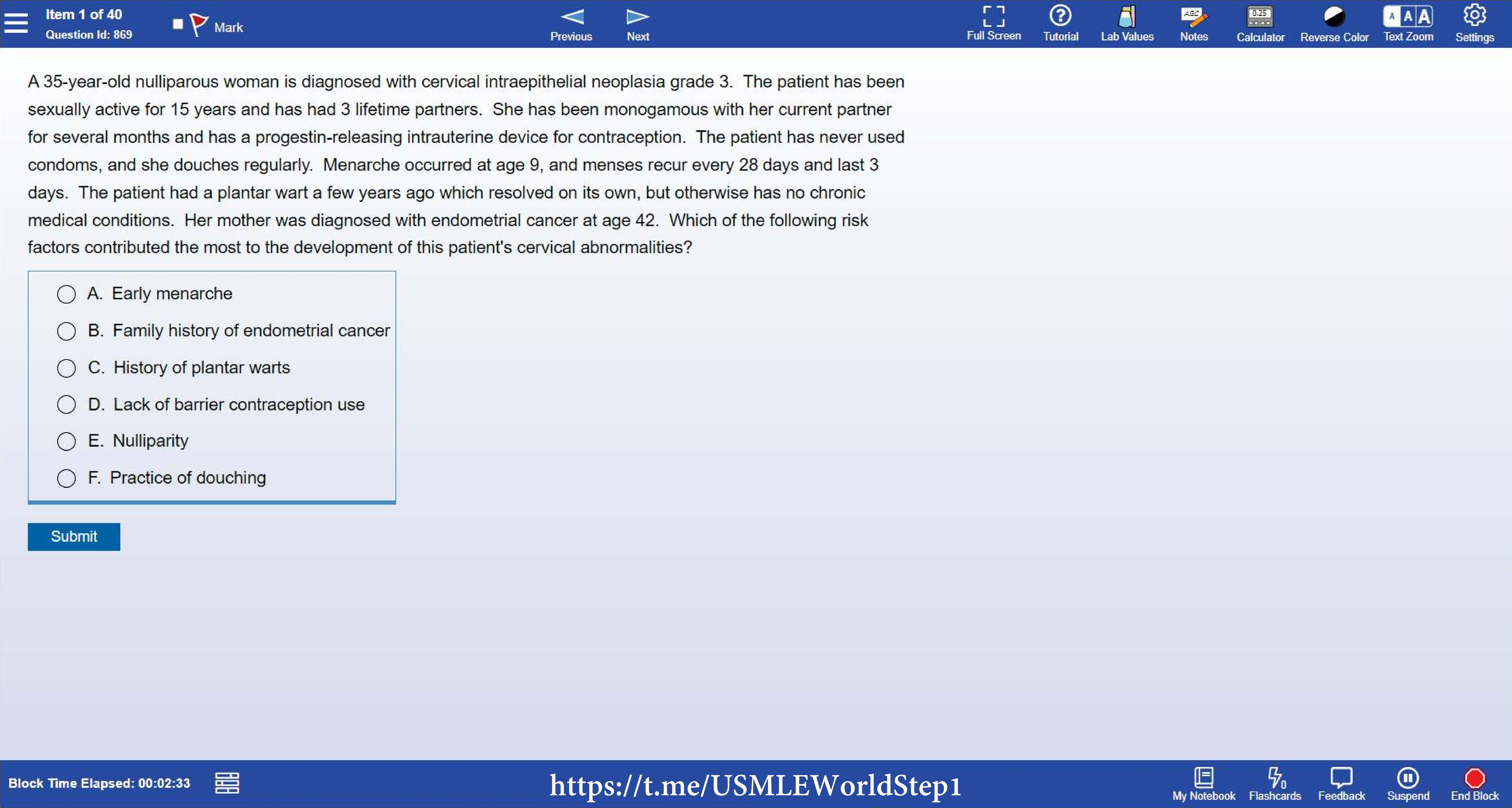
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Item 1 of 40
Question Id: 869

A 35-year-old nulliparous woman is diagnosed with cervical intraepithelial neoplasia grade 3. The patient has been sexually active for 15 years and has had 3 lifetime partners. She has been monogamous with her current partner for several months and has a progestin-releasing intrauterine device for contraception. The patient has never used condoms, and she douches regularly. Menarche occurred at age 9, and menses recur every 28 days and last 3 days. The patient had a plantar wart a few years ago which resolved on its own, but otherwise has no chronic medical conditions. Her mother was diagnosed with endometrial cancer at age 42. Which of the following risk factors contributed the most to the development of this patient's cervical abnormalities?

- ○ A. Early menarche
- ○ B. Family history of endometrial cancer
- ○ C. History of plantar warts
- ○ D. Lack of barrier contraception use
- ○ E. Nulliparity
- ○ F. Practice of douching

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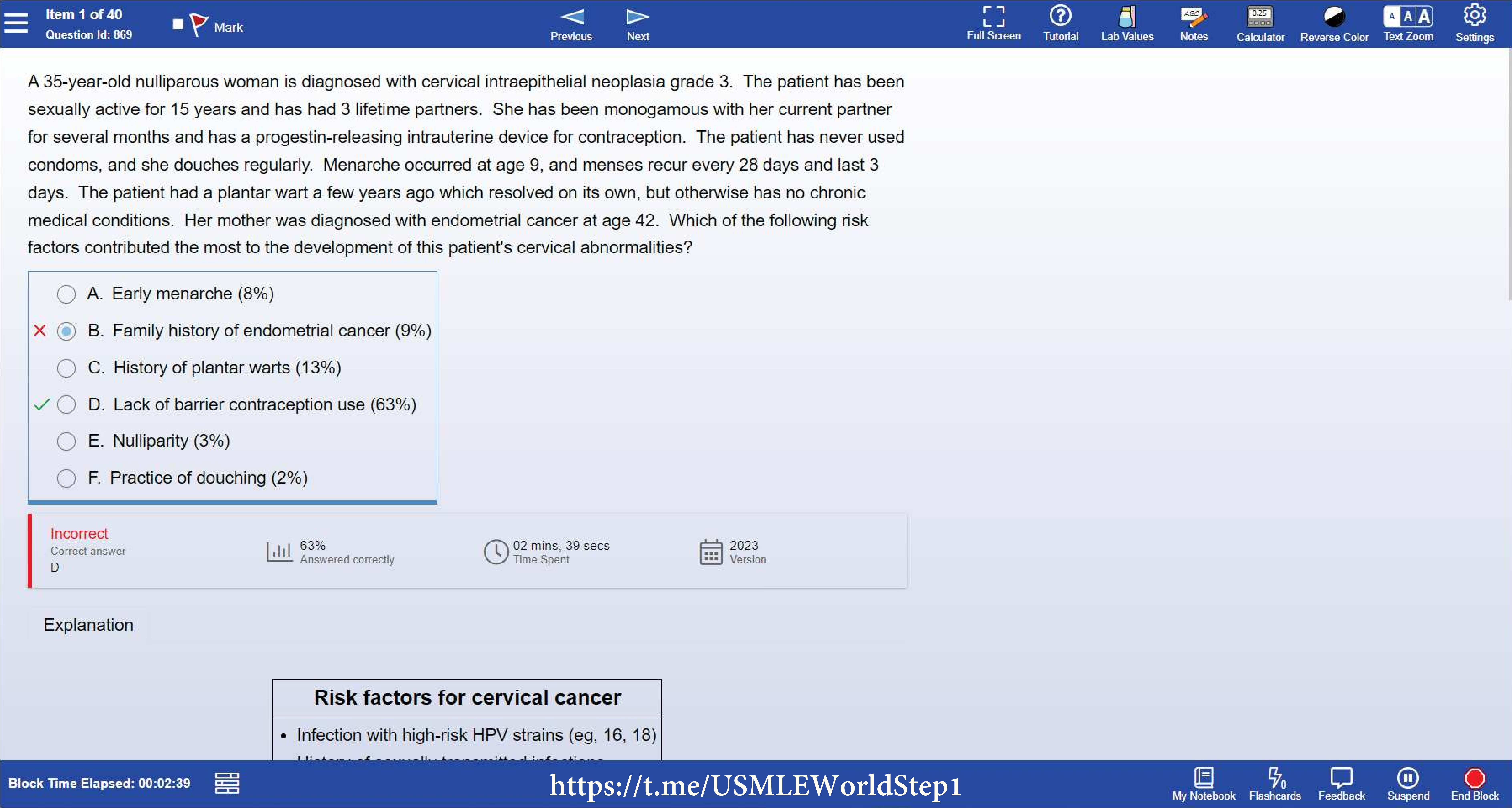
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- ○ A. Early menarche (8%)
- ✗ ● B. Family history of endometrial cancer (9%)
- ○ C. History of plantar warts (13%)
- ✓ ○ D. Lack of barrier contraception use (63%)
- ○ E. Nulliparity (3%)
- ○ F. Practice of douching (2%)

Incorrect
Correct answer
D

63%
Answered correctly

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Explanation

Risk factors for cervical cancer
• Infection with high-risk HPV strains (eg, 16, 18)

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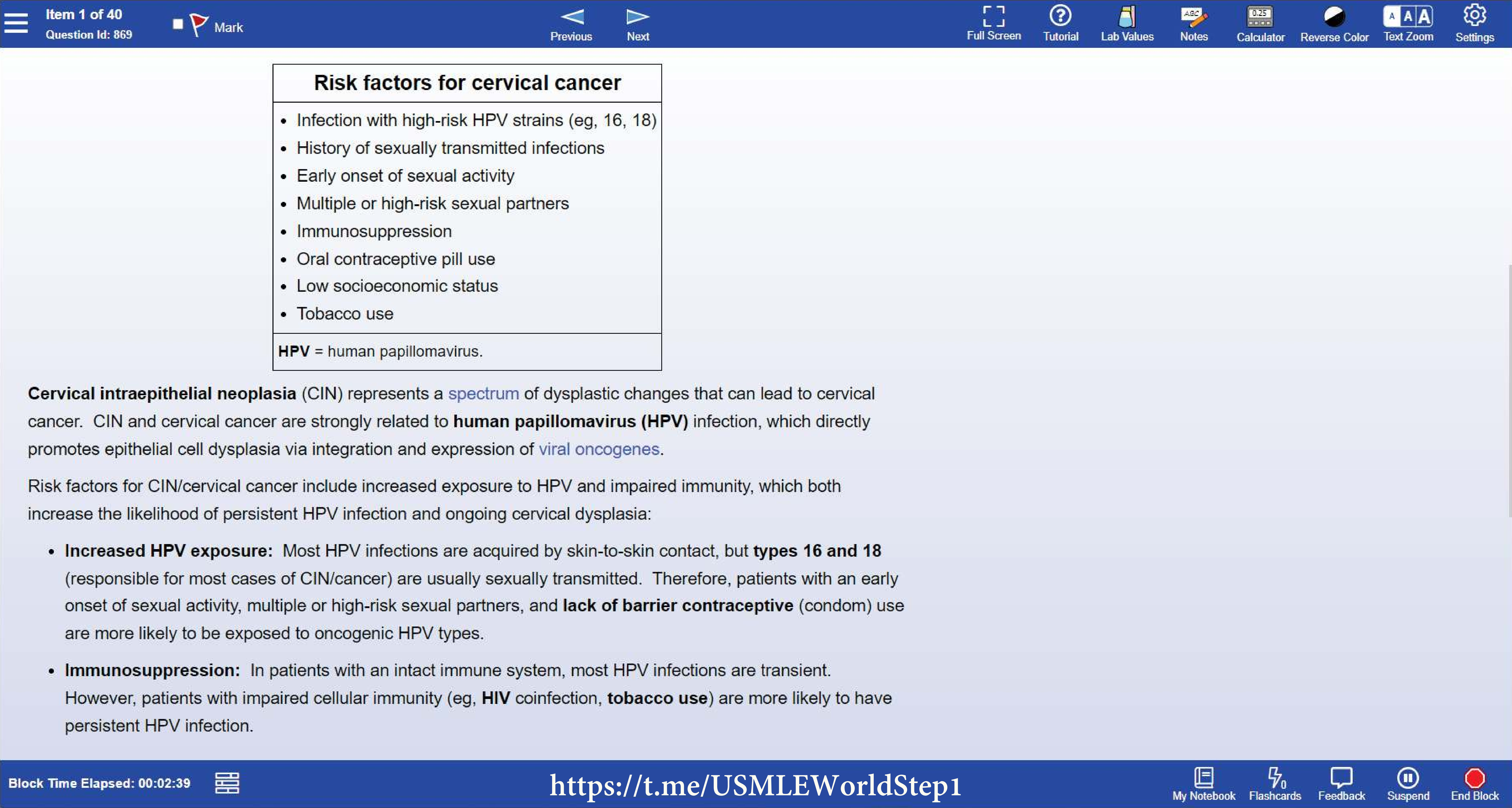
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Risk factors for cervical cancer

- Infection with high-risk HPV strains (eg, 16, 18)
- History of sexually transmitted infections
- Early onset of sexual activity
- Multiple or high-risk sexual partners
- Immunosuppression
- Oral contraceptive pill use
- Low socioeconomic status
- Tobacco use

HPV = human papillomavirus.

Cervical intraepithelial neoplasia (CIN) represents a spectrum of dysplastic changes that can lead to cervical cancer. CIN and cervical cancer are strongly related to **human papillomavirus (HPV)** infection, which directly promotes epithelial cell dysplasia via integration and expression of viral oncogenes.

Risk factors for CIN/cervical cancer include increased exposure to HPV and impaired immunity, which both increase the likelihood of persistent HPV infection and ongoing cervical dysplasia:

- **Increased HPV exposure:** Most HPV infections are acquired by skin-to-skin contact, but **types 16 and 18** (responsible for most cases of CIN/cancer) are usually sexually transmitted. Therefore, patients with an early onset of sexual activity, multiple or high-risk sexual partners, and **lack of barrier contraceptive** (condom) use are more likely to be exposed to oncogenic HPV types.
- **Immunosuppression:** In patients with an intact immune system, most HPV infections are transient. However, patients with impaired cellular immunity (eg, **HIV** coinfection, **tobacco use**) are more likely to have persistent HPV infection.

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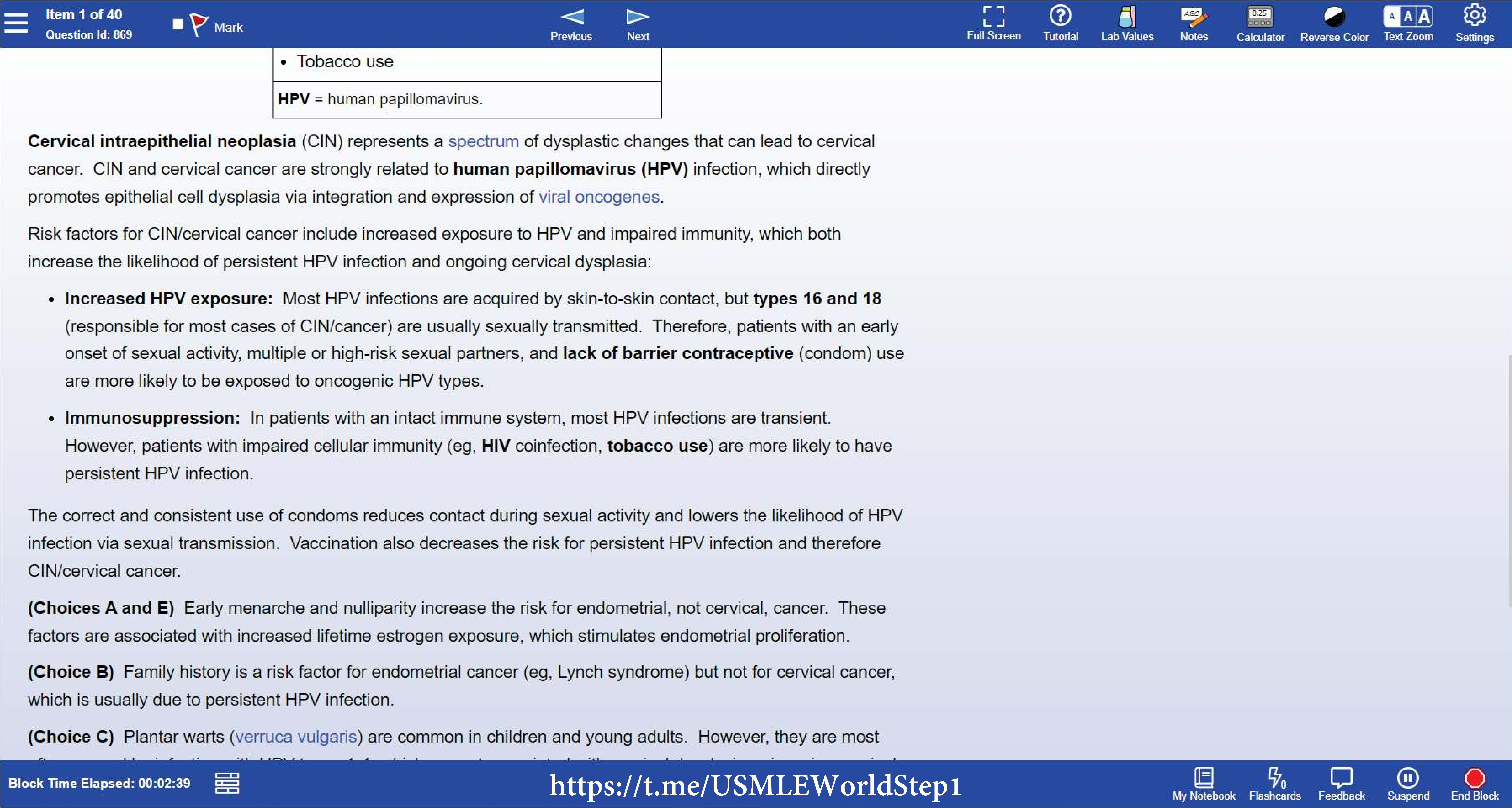

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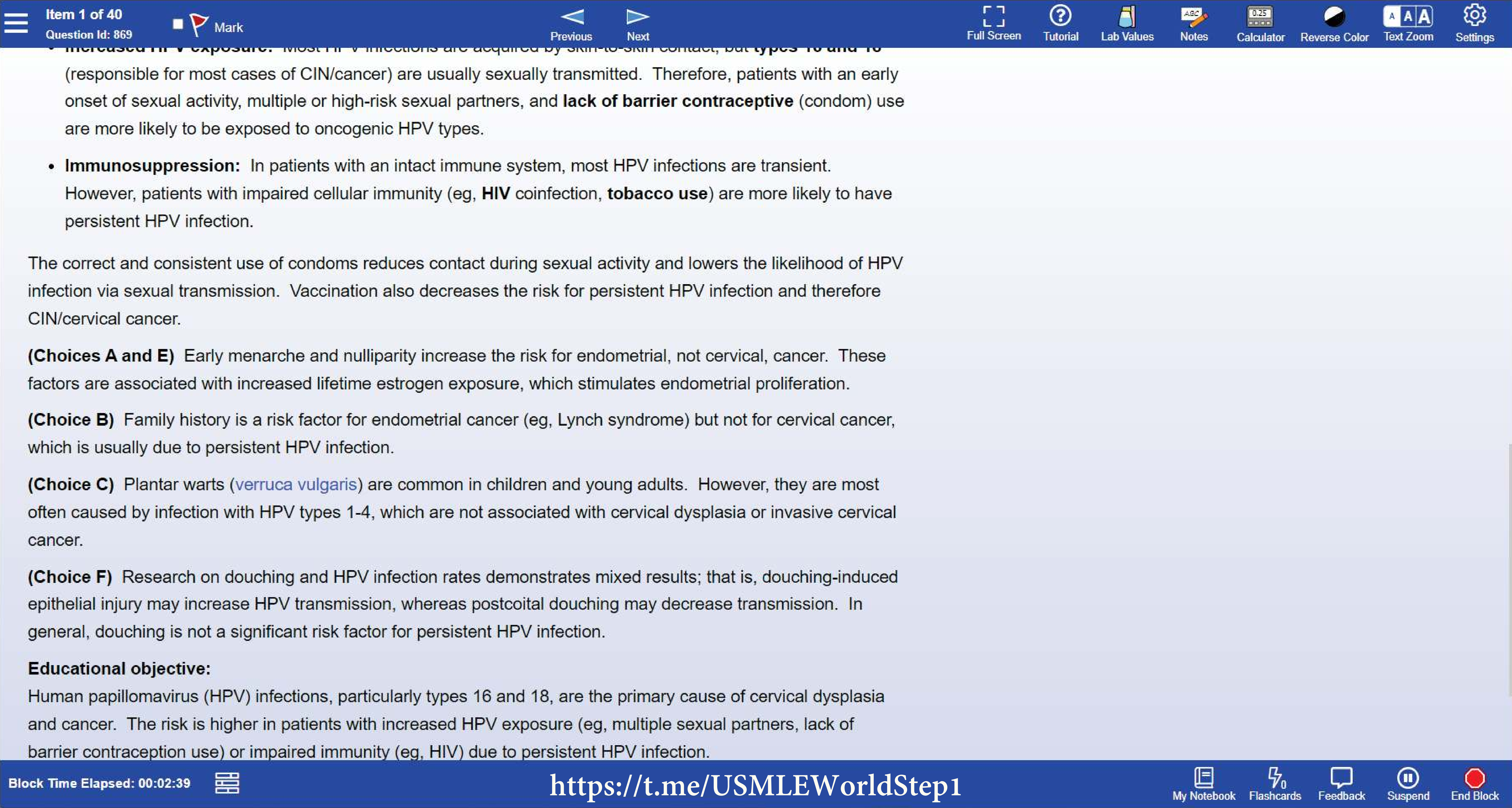
- **Immunosuppression:** In patients with an intact immune system, most HPV infections are transient. However, patients with impaired cellular immunity (eg, **HIV** coinfection, **tobacco use**) are more likely to have persistent HPV infection.

The correct and consistent use of condoms reduces contact during sexual activity and lowers the likelihood of HPV infection via sexual transmission. Vaccination also decreases the risk for persistent HPV infection and therefore CIN/cervical cancer.

(Choices A and E) Early menarche and nulliparity increase the risk for endometrial, not cervical, cancer. These factors are associated with increased lifetime estrogen exposure, which stimulates endometrial proliferation.

(Choice B) Family history is a risk factor for endometrial cancer (eg, Lynch syndrome) but not for cervical cancer, which is usually due to persistent HPV infection.

(Choice C) Plantar warts (verruca vulgaris) are common in children and young adults. However, they are most



- **Increased HPV exposure:** Most HPV infections are acquired by skin-to-skin contact, but **types 16 and 18** (responsible for most cases of CIN/cancer) are usually sexually transmitted. Therefore, patients with an early onset of sexual activity, multiple or high-risk sexual partners, and **lack of barrier contraceptive** (condom) use are more likely to be exposed to oncogenic HPV types.
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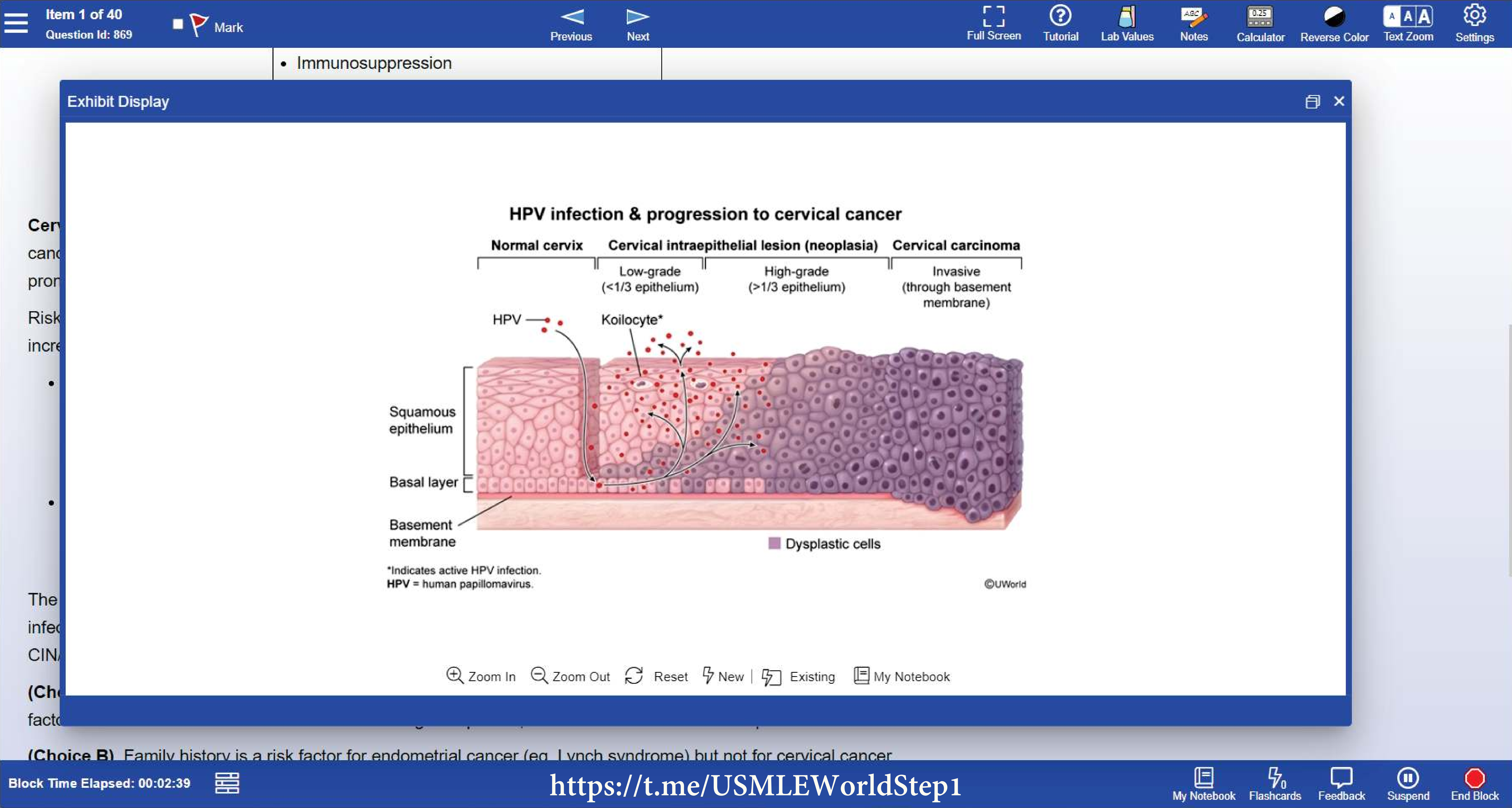
(Choice B) Family history is a risk factor for endometrial cancer (eg, Lynch syndrome) but not for cervical cancer, which is usually due to persistent HPV infection.

(Choice C) Plantar warts (verruca vulgaris) are common in children and young adults. However, they are most often caused by infection with HPV types 1-4, which are not associated with cervical dysplasia or invasive cervical cancer.

(Choice F) Research on douching and HPV infection rates demonstrates mixed results; that is, douching-induced epithelial injury may increase HPV transmission, whereas postcoital douching may decrease transmission. In general, douching is not a significant risk factor for persistent HPV infection.

Educational objective:
Human papillomavirus (HPV) infections, particularly types 16 and 18, are the primary cause of cervical dysplasia and cancer. The risk is higher in patients with increased HPV exposure (eg, multiple sexual partners, lack of barrier contraception use) or impaired immunity (eg, HIV) due to persistent HPV infection.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- Immunosuppression

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(Choice B) Family history is a risk factor for endometrial cancer (eg, Lynch syndrome) but not for cervical cancer

HPV infection & progression to cervical cancer

Normal cervix
Cervical intraepithelial lesion (neoplasia)
Cervical carcinoma
Low-grade
(<1/3 epithelium)
High-grade
(>1/3 epithelium)
Invasive
(through basement
membrane)
HPV
Koilocyte*
Squamous
epithelium
Basal layer
Basement
membrane
Dysplastic cells

*Indicates active HPV infection.
HPV = human papillomavirus.

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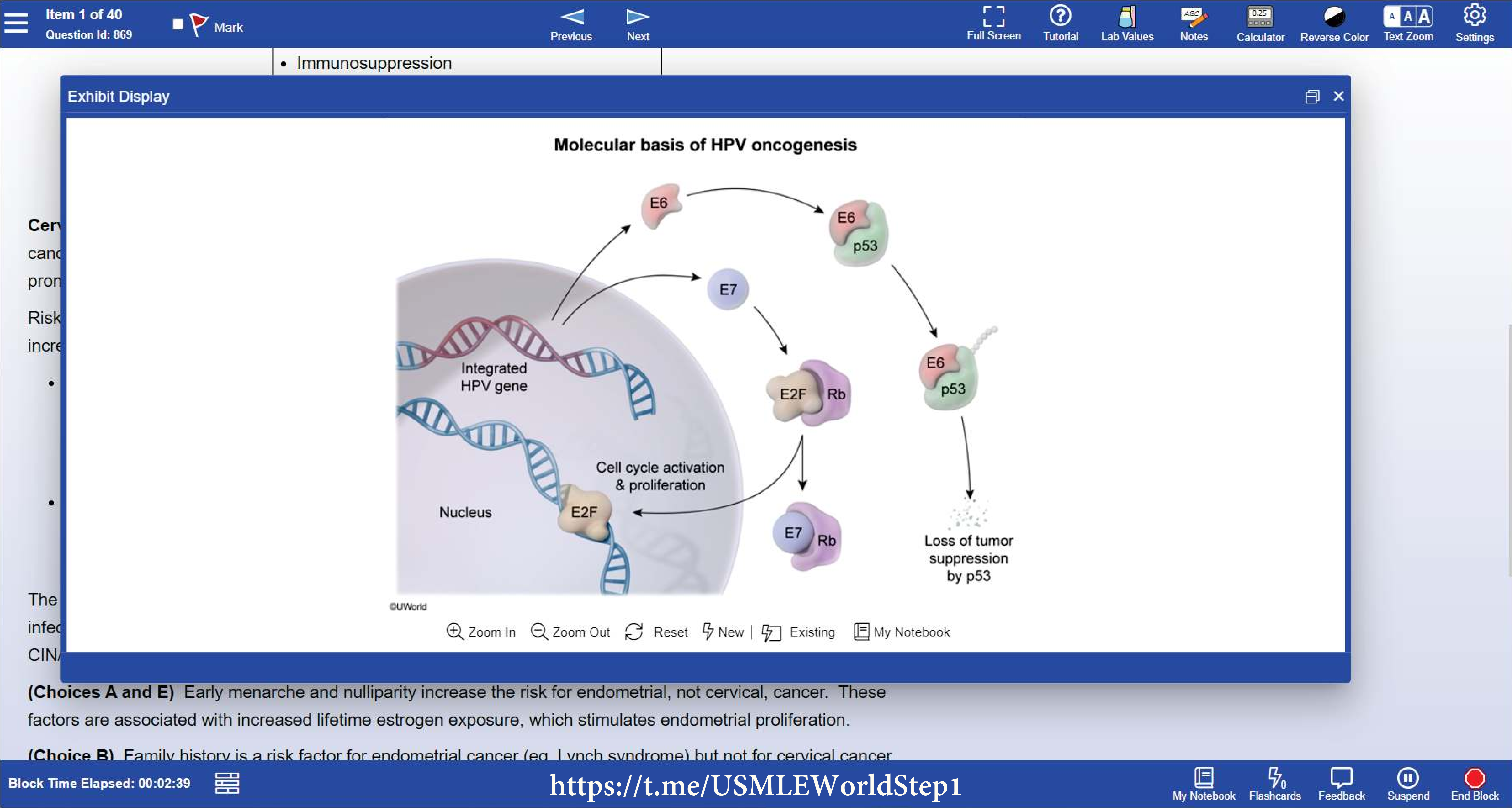
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- Immunosuppression

Molecular basis of HPV oncogenesis

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(Choices A and E) Early menarche and nulliparity increase the risk for endometrial, not cervical, cancer. These factors are associated with increased lifetime estrogen exposure, which stimulates endometrial proliferation.

(Choice B) Family history is a risk factor for endometrial cancer (eg, Lynch syndrome) but not for cervical cancer

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are more likely to be exposed to oncogenic HPV types.

- **Immunosuppression:** In patients with an intact immune system, most HPV infections are transient

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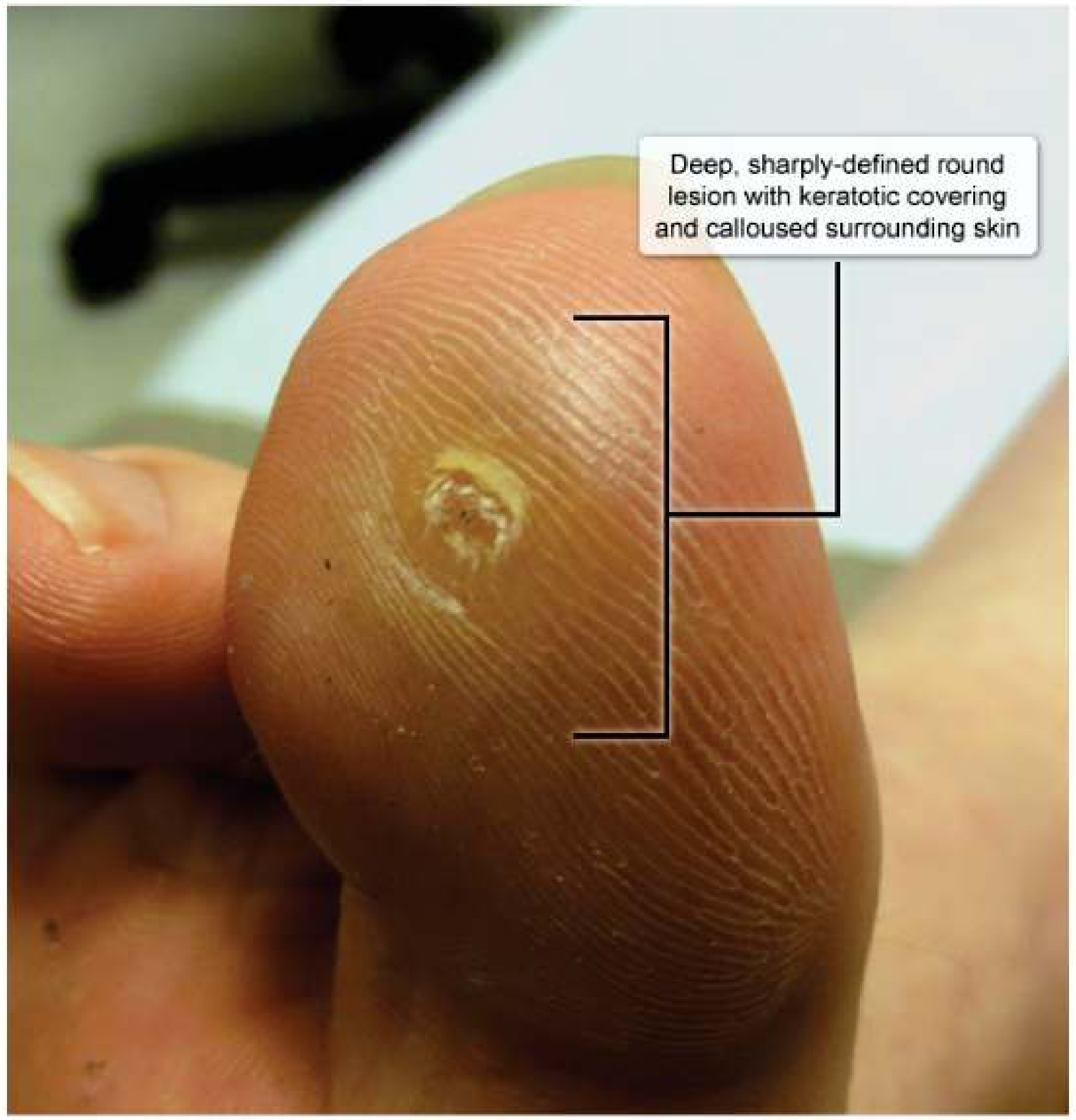
Plantar wart


Deep, sharply-defined round lesion with keratotic covering and calloused surrounding skin

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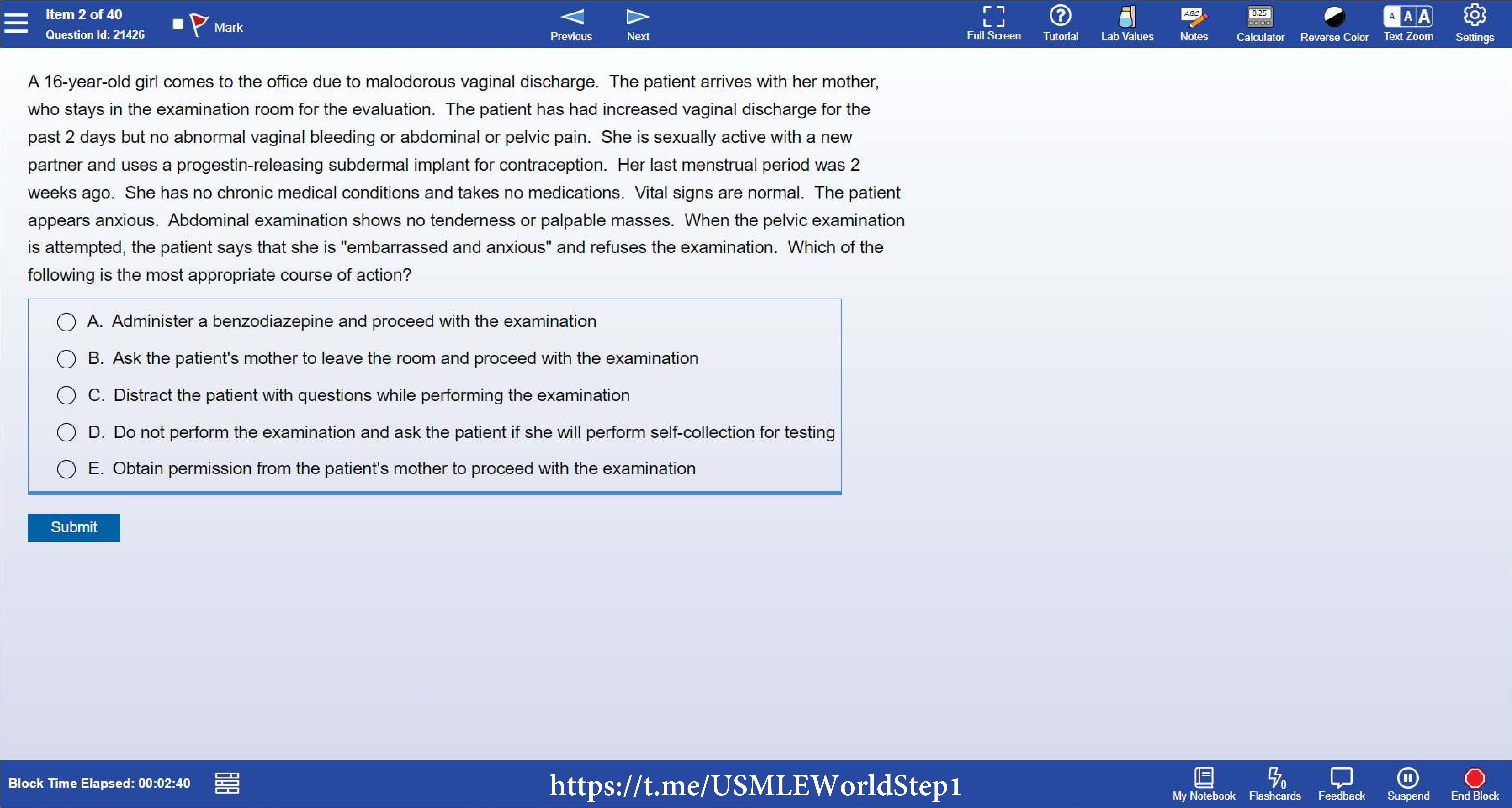
- HPV infection and cervical neoplasia: associated risk factors.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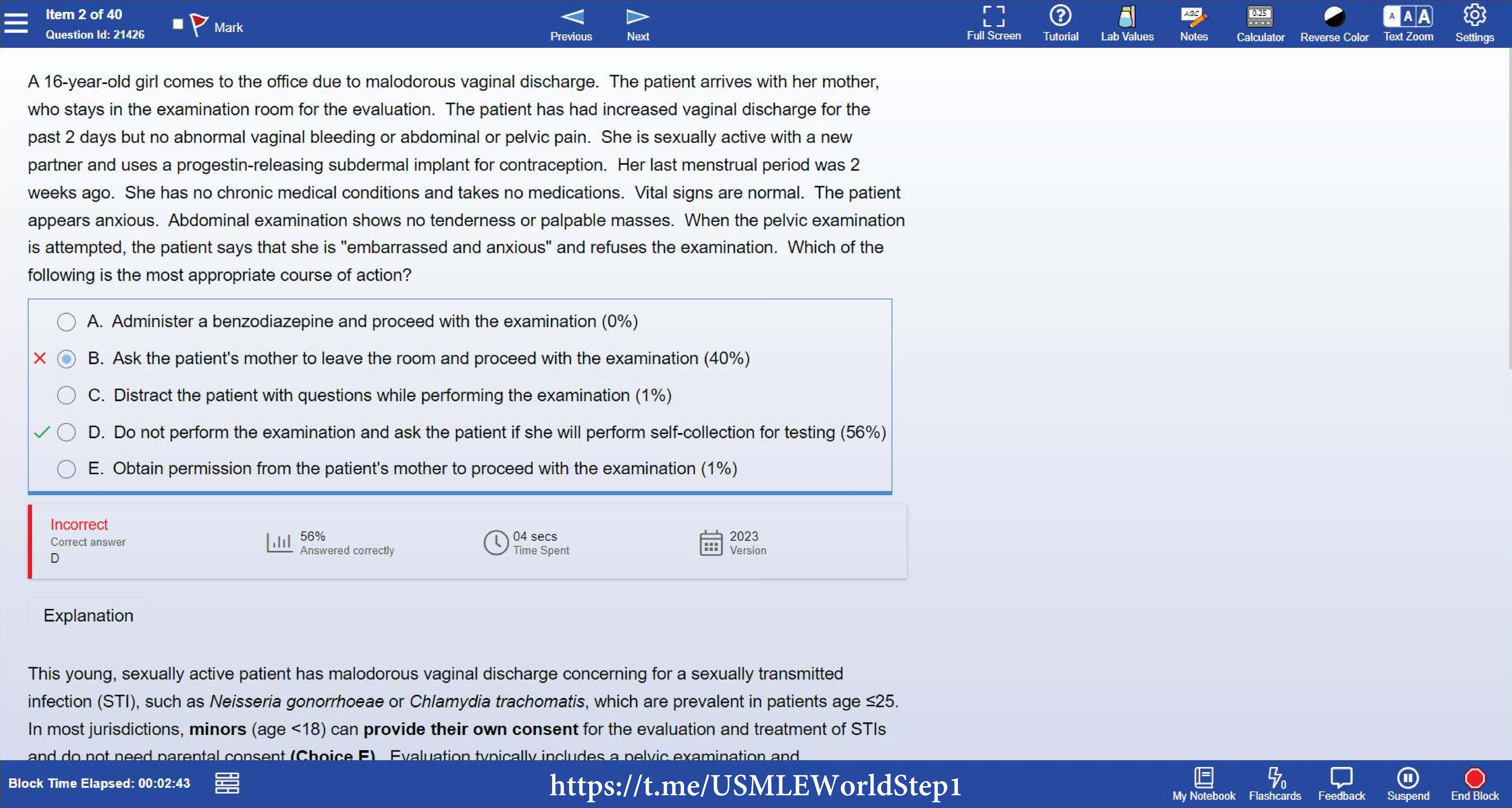
A 16-year-old girl comes to the office due to malodorous vaginal discharge. The patient arrives with her mother, who stays in the examination room for the evaluation. The patient has had increased vaginal discharge for the past 2 days but no abnormal vaginal bleeding or abdominal or pelvic pain. She is sexually active with a new partner and uses a progestin-releasing subdermal implant for contraception. Her last menstrual period was 2 weeks ago. She has no chronic medical conditions and takes no medications. Vital signs are normal. The patient appears anxious. Abdominal examination shows no tenderness or palpable masses. When the pelvic examination is attempted, the patient says that she is "embarrassed and anxious" and refuses the examination. Which of the following is the most appropriate course of action?

- ○ A. Administer a benzodiazepine and proceed with the examination
- ○ B. Ask the patient's mother to leave the room and proceed with the examination
- ○ C. Distract the patient with questions while performing the examination
- ○ D. Do not perform the examination and ask the patient if she will perform self-collection for testing
- ○ E. Obtain permission from the patient's mother to proceed with the examination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- ○ A. Administer a benzodiazepine and proceed with the examination (0%)
- ✗ ● B. Ask the patient's mother to leave the room and proceed with the examination (40%)
- ○ C. Distract the patient with questions while performing the examination (1%)
- ✓ ○ D. Do not perform the examination and ask the patient if she will perform self-collection for testing (56%)
- ○ E. Obtain permission from the patient's mother to proceed with the examination (1%)

Incorrect
Correct answer
D

56%
Answered correctly

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Time Spent

2023
Version

Explanation

This young, sexually active patient has malodorous vaginal discharge concerning for a sexually transmitted infection (STI), such as *Neisseria gonorrhoeae* or *Chlamydia trachomatis*, which are prevalent in patients age ≤25. In most jurisdictions, **minors** (age <18) can **provide their own consent** for the evaluation and treatment of STIs and do not need parental consent **(Choice E)**. Evaluation typically includes a pelvic examination and

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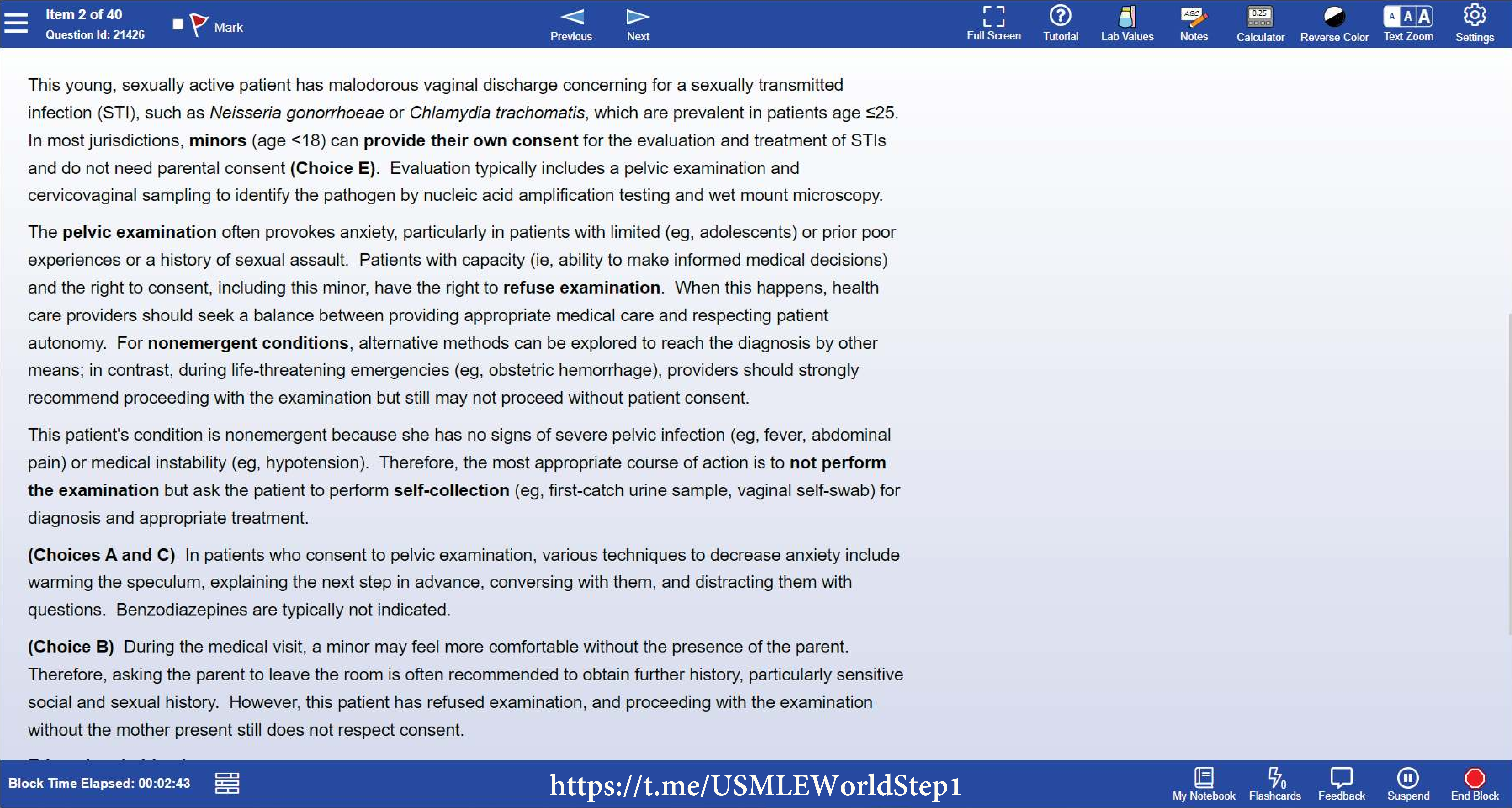

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The **pelvic examination** often provokes anxiety, particularly in patients with limited (eg, adolescents) or prior poor experiences or a history of sexual assault. Patients with capacity (ie, ability to make informed medical decisions) and the right to consent, including this minor, have the right to **refuse examination**. When this happens, health care providers should seek a balance between providing appropriate medical care and respecting patient autonomy. For **nonemergent conditions**, alternative methods can be explored to reach the diagnosis by other means; in contrast, during life-threatening emergencies (eg, obstetric hemorrhage), providers should strongly recommend proceeding with the examination but still may not proceed without patient consent.

This patient's condition is nonemergent because she has no signs of severe pelvic infection (eg, fever, abdominal pain) or medical instability (eg, hypotension). Therefore, the most appropriate course of action is to **not perform the examination** but ask the patient to perform **self-collection** (eg, first-catch urine sample, vaginal self-swab) for diagnosis and appropriate treatment.

(Choices A and C) In patients who consent to pelvic examination, various techniques to decrease anxiety include warming the speculum, explaining the next step in advance, conversing with them, and distracting them with questions. Benzodiazepines are typically not indicated.

(Choice B) During the medical visit, a minor may feel more comfortable without the presence of the parent. Therefore, asking the parent to leave the room is often recommended to obtain further history, particularly sensitive social and sexual history. However, this patient has refused examination, and proceeding with the examination without the mother present still does not respect consent.

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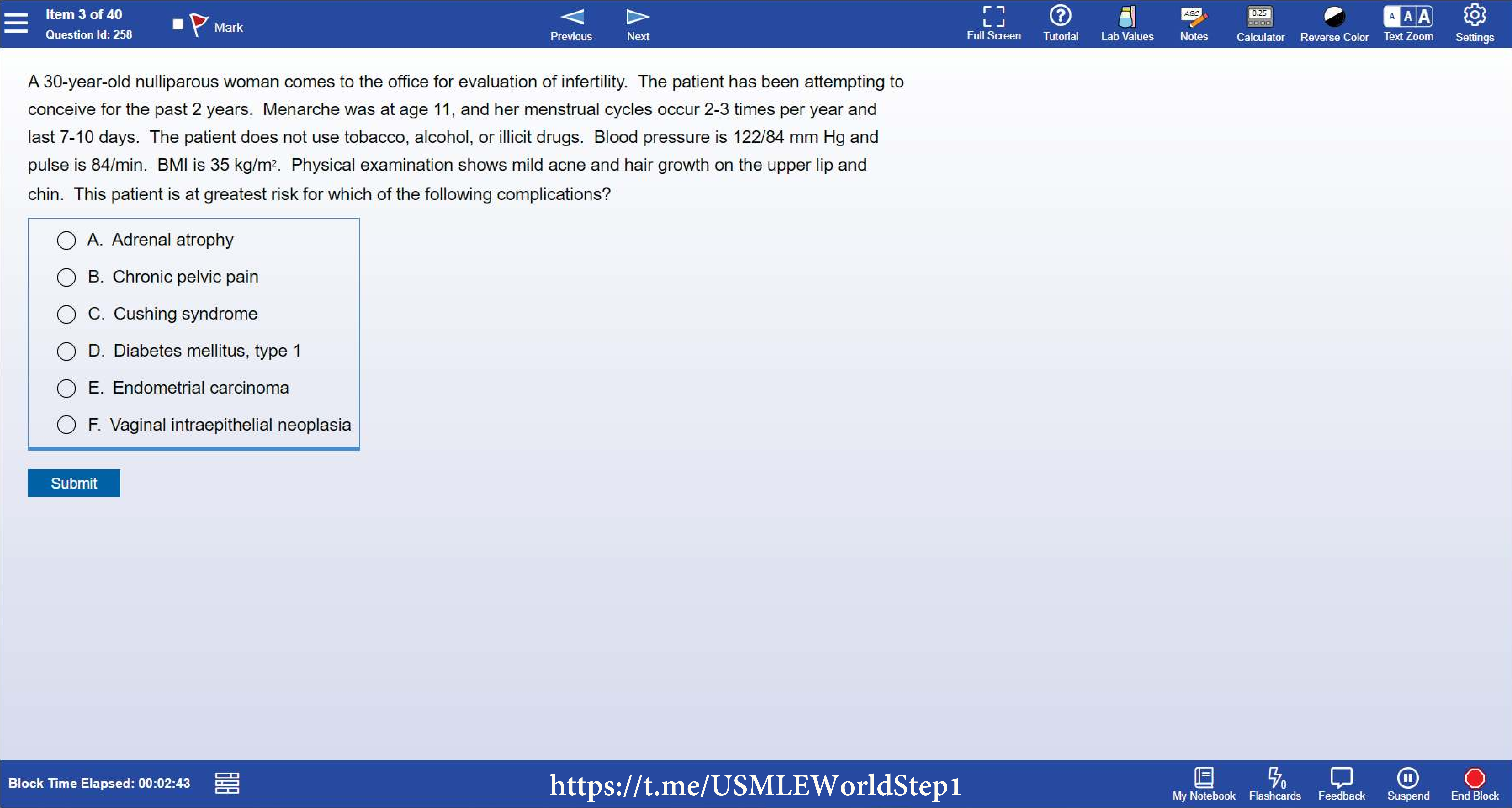
Educational objective:
Patients with the right to consent can refuse portions of the medical evaluation (eg, pelvic examination). In nonemergent cases, alternative methods for achieving the diagnosis and providing appropriate treatment (eg, patient self-collection) are appropriate.

References

- Informed consent in decision-making in pediatric practice.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A 30-year-old nulliparous woman comes to the office for evaluation of infertility. The patient has been attempting to conceive for the past 2 years. Menarche was at age 11, and her menstrual cycles occur 2-3 times per year and last 7-10 days. The patient does not use tobacco, alcohol, or illicit drugs. Blood pressure is 122/84 mm Hg and pulse is 84/min. BMI is 35 kg/m^2. Physical examination shows mild acne and hair growth on the upper lip and chin. This patient is at greatest risk for which of the following complications?

○ A. Adrenal atrophy
○ B. Chronic pelvic pain
○ C. Cushing syndrome
○ D. Diabetes mellitus, type 1
○ E. Endometrial carcinoma
○ F. Vaginal intraepithelial neoplasia

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○ A. Adrenal atrophy (4%)
○ B. Chronic pelvic pain (9%)
× ● C. Cushing syndrome (9%)
○ D. Diabetes mellitus, type 1 (9%)
✓ ○ E. Endometrial carcinoma (65%)
○ F. Vaginal intraepithelial neoplasia (1%)

Incorrect
Correct answer
E

65%
Answered correctly

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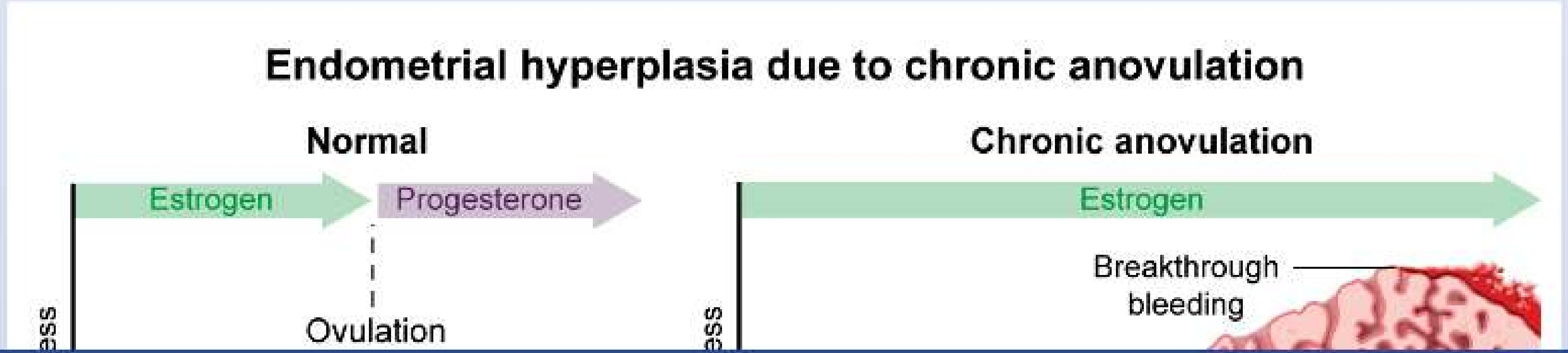
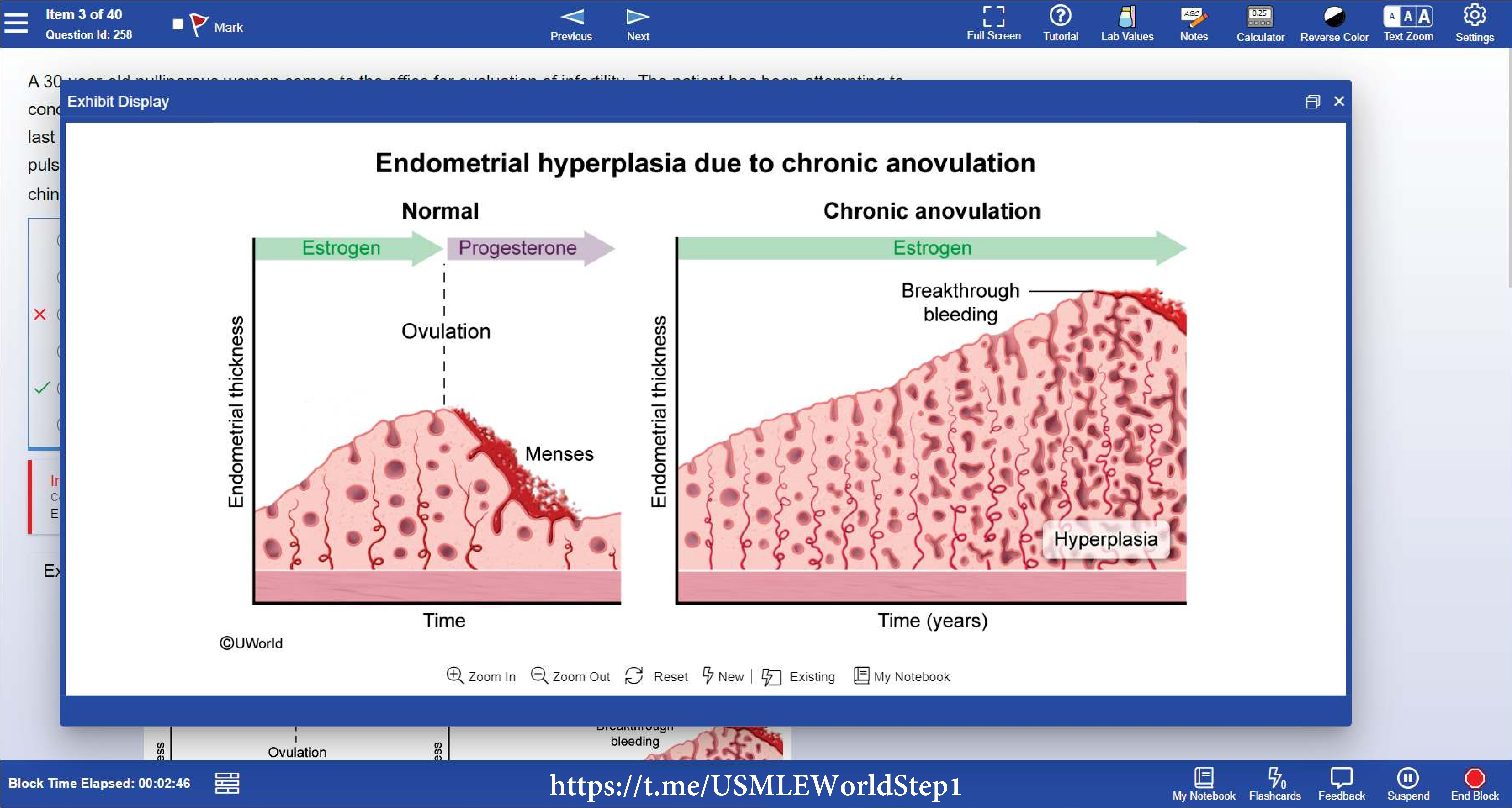
Explanation


Endometrial hyperplasia due to chronic anovulation
Normal
Estrogen
Progesterone
Ovulation
Chronic anovulation
Estrogen
Breakthrough bleeding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Endometrial hyperplasia due to chronic anovulation

Normal
Estrogen
Progesterone
Ovulation
Menses
Endometrial thickness
Time
Chronic anovulation
Estrogen
Breakthrough bleeding
Hyperplasia
Endometrial thickness
Time (years)

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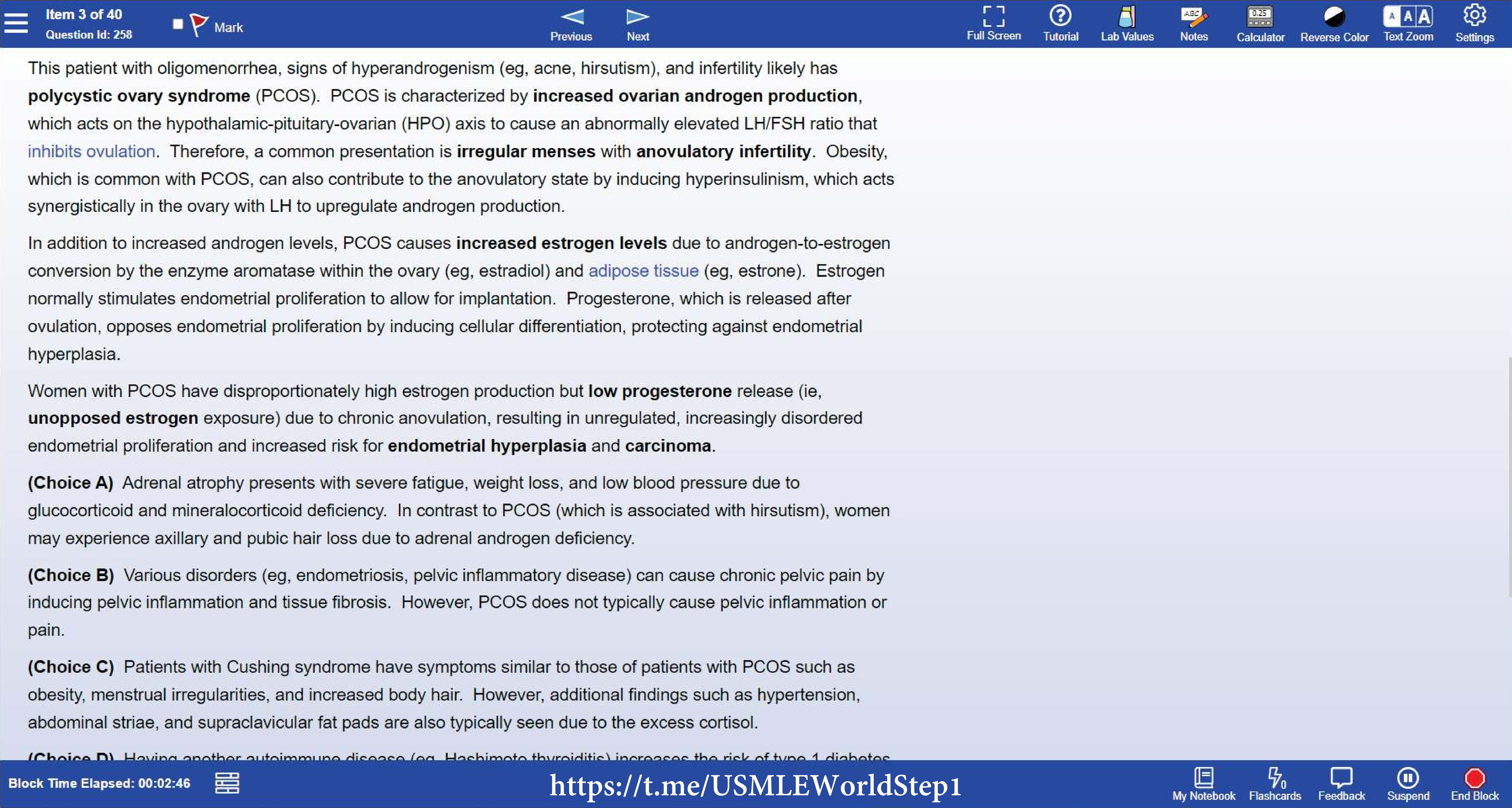


This patient with oligomenorrhea, signs of hyperandrogenism (eg, acne, hirsutism), and infertility likely has **polycystic ovary syndrome** (PCOS). PCOS is characterized by **increased ovarian androgen production**, which acts on the hypothalamic-pituitary-ovarian (HPO) axis to cause an abnormally elevated LH/FSH ratio that inhibits ovulation. Therefore, a common presentation is **irregular menses** with **anovulatory infertility**. Obesity, which is common with PCOS, can also contribute to the anovulatory state by inducing hyperinsulinism, which acts synergistically in the ovary with LH to upregulate androgen production.

In addition to increased androgen levels, PCOS causes **increased estrogen levels** due to androgen-to-estrogen conversion by the enzyme aromatase within the ovary (eg, estradiol) and adipose tissue (eg, estrone). Estrogen normally stimulates endometrial proliferation to allow for implantation. Progesterone, which is released after ovulation, opposes endometrial proliferation by inducing cellular differentiation, protecting against endometrial hyperplasia.

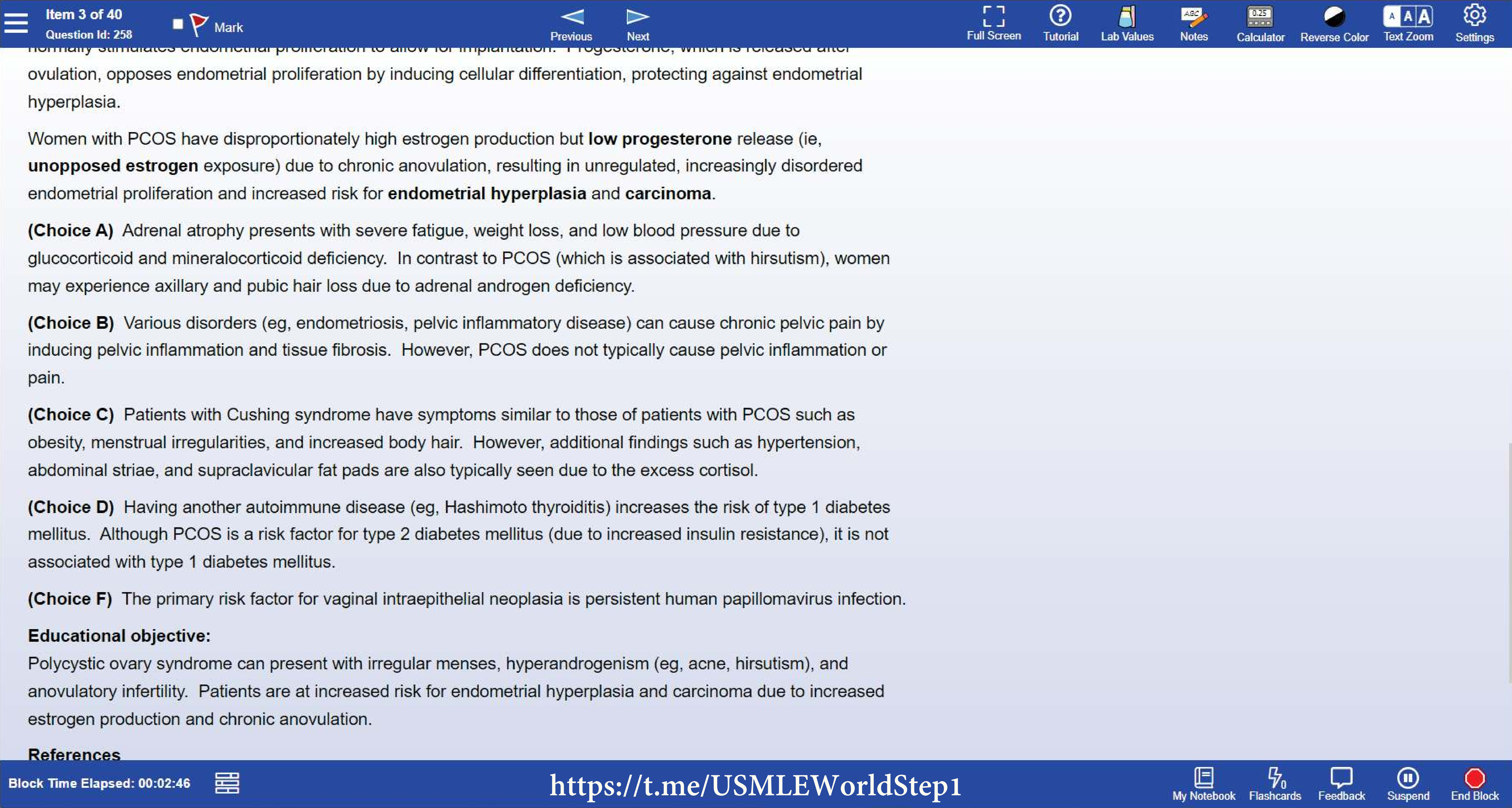
Women with PCOS have disproportionately high estrogen production but **low progesterone** release (ie, **unopposed estrogen** exposure) due to chronic anovulation, resulting in unregulated, increasingly disordered endometrial proliferation and increased risk for **endometrial hyperplasia** and **carcinoma**.

(Choice A) Adrenal atrophy presents with severe fatigue, weight loss, and low blood pressure due to glucocorticoid and mineralocorticoid deficiency. In contrast to PCOS (which is associated with hirsutism), women may experience axillary and pubic hair loss due to adrenal androgen deficiency.

(Choice B) Various disorders (eg, endometriosis, pelvic inflammatory disease) can cause chronic pelvic pain by inducing pelvic inflammation and tissue fibrosis. However, PCOS does not typically cause pelvic inflammation or pain.

(Choice C) Patients with Cushing syndrome have symptoms similar to those of patients with PCOS such as obesity, menstrual irregularities, and increased body hair. However, additional findings such as hypertension, abdominal striae, and supraclavicular fat pads are also typically seen due to the excess cortisol.

(Choice D) Having another autoimmune disease (eg, Hashimoto thyroiditis) increases the risk of type 1 diabetes



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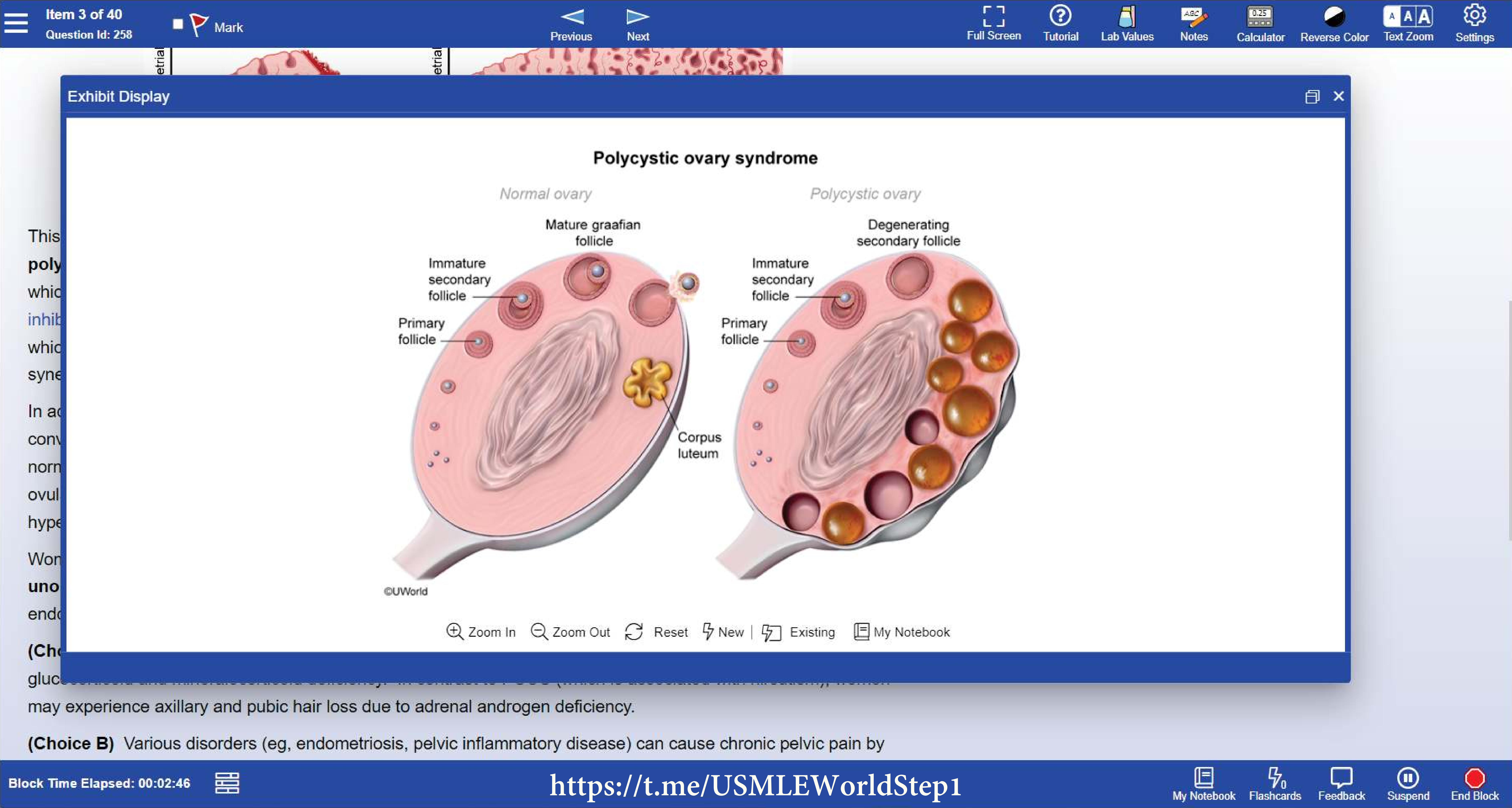
(Choice D) Having another autoimmune disease (eg, Hashimoto thyroiditis) increases the risk of type 1 diabetes mellitus. Although PCOS is a risk factor for type 2 diabetes mellitus (due to increased insulin resistance), it is not associated with type 1 diabetes mellitus.

(Choice F) The primary risk factor for vaginal intraepithelial neoplasia is persistent human papillomavirus infection.

Educational objective:
Polycystic ovary syndrome can present with irregular menses, hyperandrogenism (eg, acne, hirsutism), and anovulatory infertility. Patients are at increased risk for endometrial hyperplasia and carcinoma due to increased estrogen production and chronic anovulation.

References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Normal ovary
Polycystic ovary
Mature graafian follicle
Immature secondary follicle
Primary follicle
Corpus luteum
Degenerating secondary follicle
Immature secondary follicle
Primary follicle
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End Block

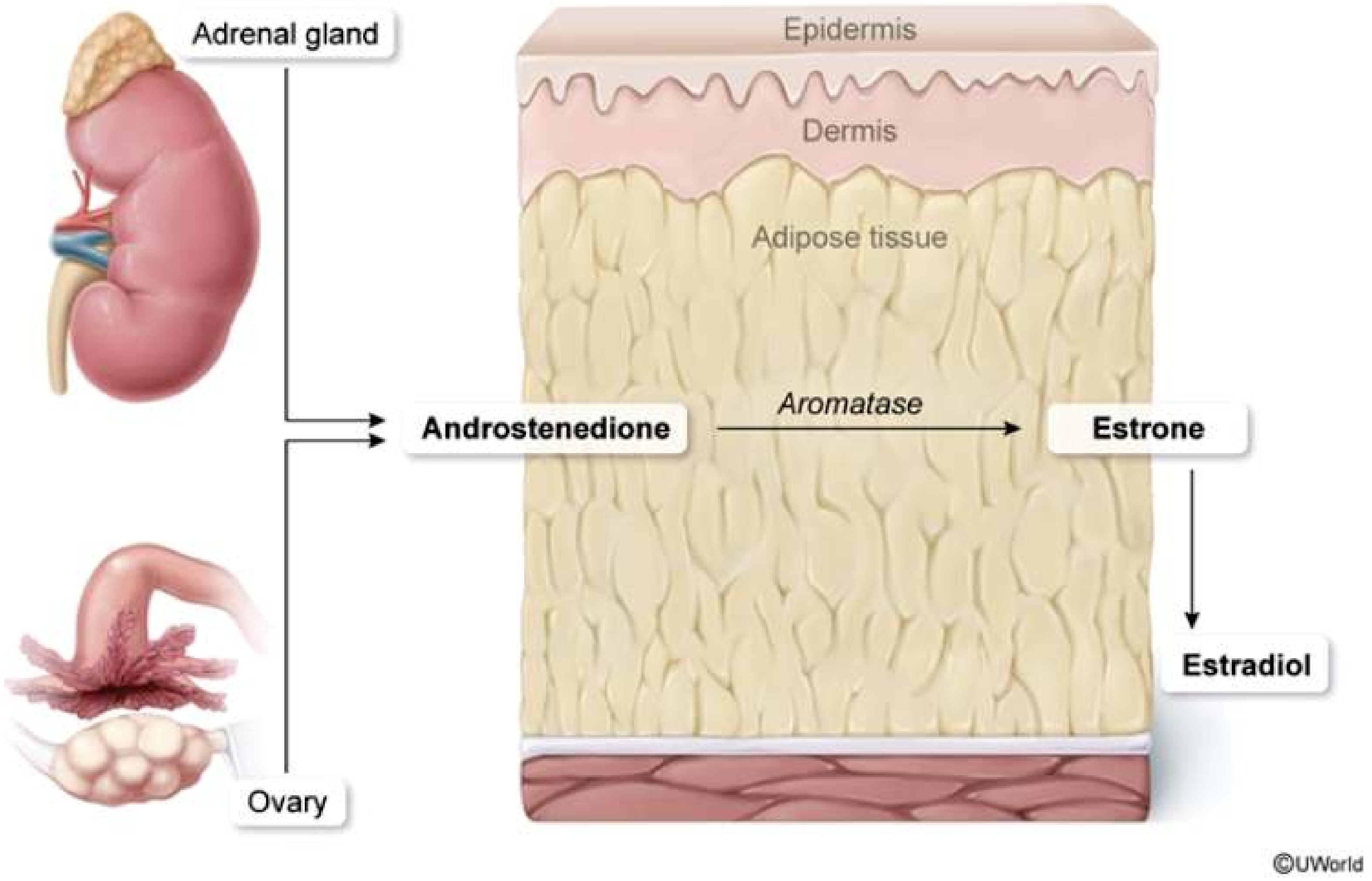
Polycystic ovary syndrome

may experience axillary and pubic hair loss due to adrenal androgen deficiency.

(Choice B) Various disorders (eg, endometriosis, pelvic inflammatory disease) can cause chronic pelvic pain by

Exhibit Display

Peripheral estrogen conversion in adipose tissue


Adrenal gland
Epidermis
Dermis
Adipose tissue
Androstenedione
Aromatase
Estrone
Estradiol
Ovary
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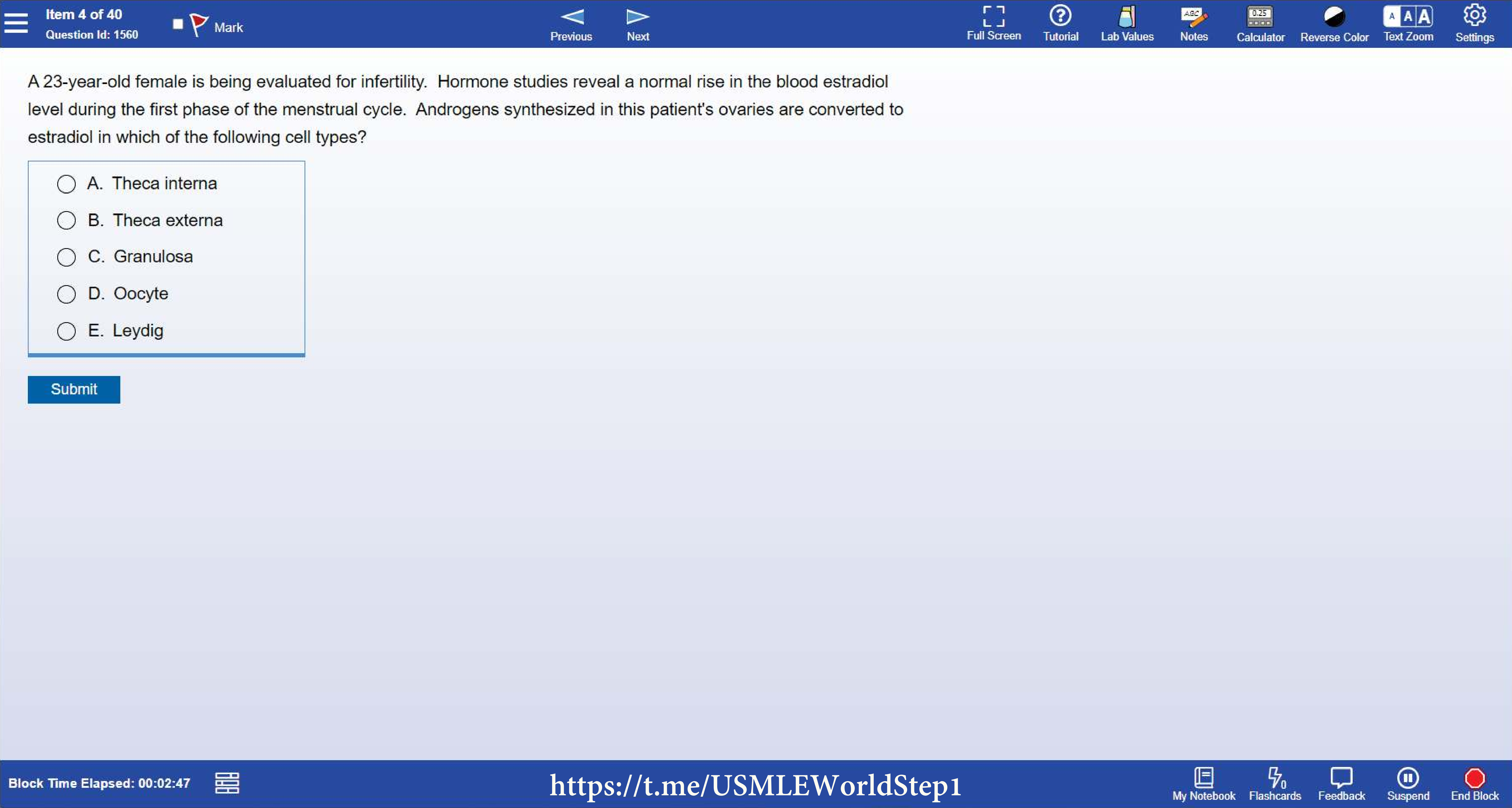
may experience axillary and pubic hair loss due to adrenal androgen deficiency.

(Choice B) Various disorders (eg, endometriosis, pelvic inflammatory disease) can cause chronic pelvic pain by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Item 4 of 40
Question Id: 1560

A 23-year-old female is being evaluated for infertility. Hormone studies reveal a normal rise in the blood estradiol level during the first phase of the menstrual cycle. Androgens synthesized in this patient's ovaries are converted to estradiol in which of the following cell types?

○ A. Theca interna
○ B. Theca externa
○ C. Granulosa
○ D. Oocyte
○ E. Leydig

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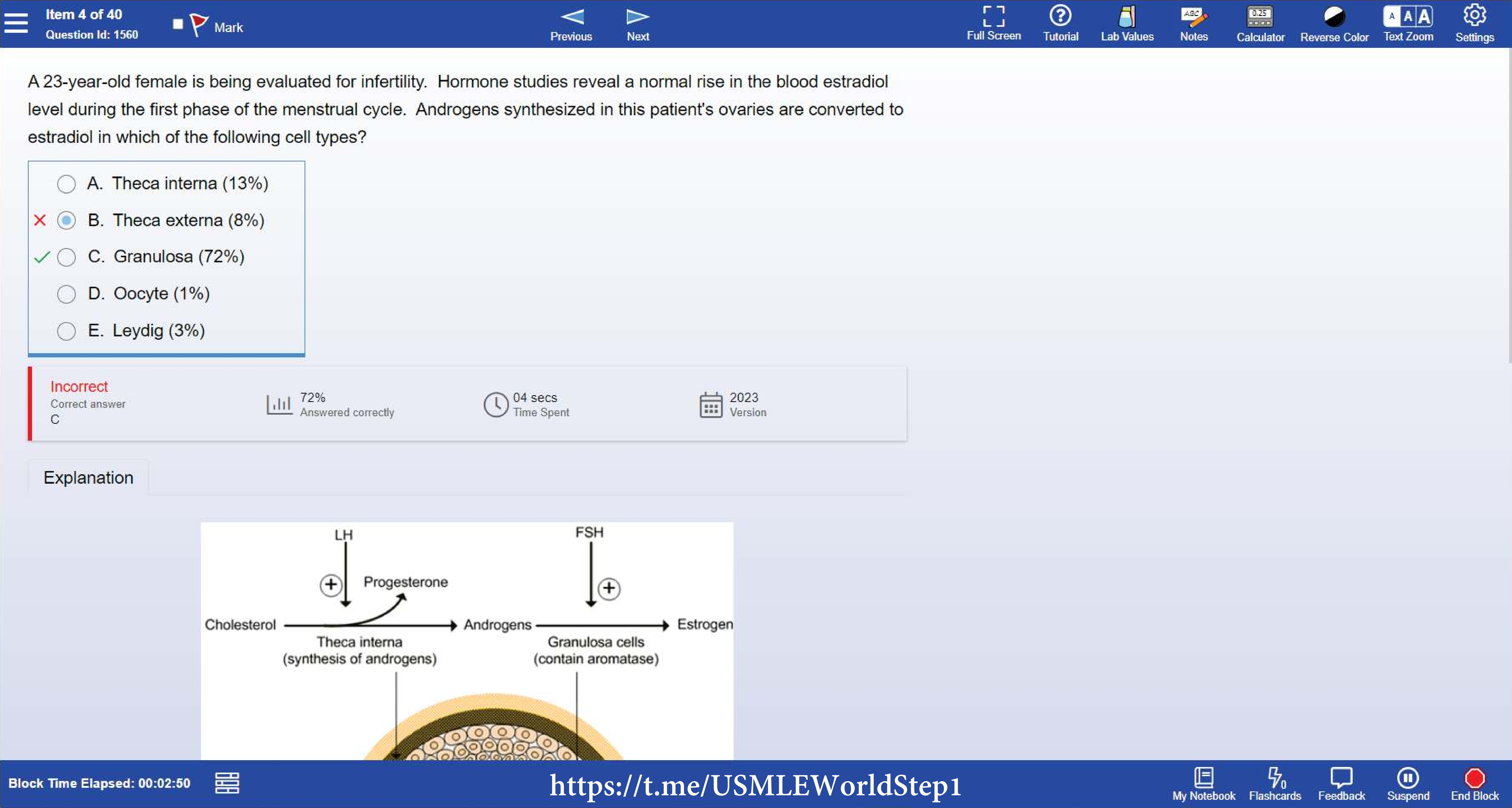
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Question Id: 1560
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Settings
LH
Progesterone
FSH
Cholesterol
Androgens
Estrogen
Theca interna
(synthesis of androgens)
Granulosa cells
(contain aromatase)
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A 23-year-old female is being evaluated for infertility. Hormone studies reveal a normal rise in the blood estradiol level during the first phase of the menstrual cycle. Androgens synthesized in this patient's ovaries are converted to estradiol in which of the following cell types?

○ A. Theca interna (13%)
✗ ● B. Theca externa (8%)
✓ ○ C. Granulosa (72%)
○ D. Oocyte (1%)
○ E. Leydig (3%)

Incorrect
Correct answer
C

72%
Answered correctly

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Explanation

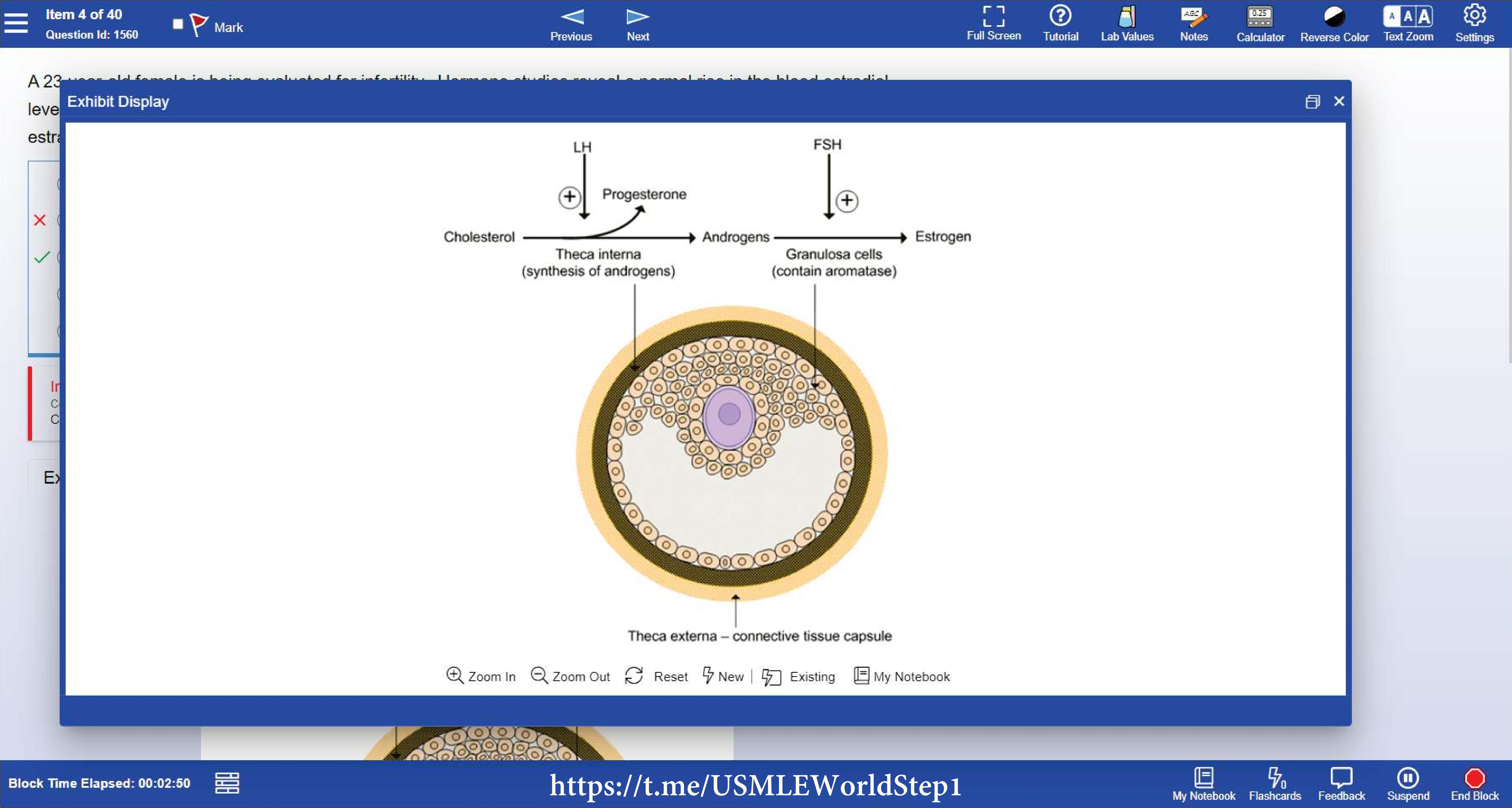
Item 4 of 40
Question Id: 1560
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Exhibit Display
LH
FSH
Progesterone
Cholesterol
Androgens
Estrogen
Theca interna
(synthesis of androgens)
Granulosa cells
(contain aromatase)
Theca externa – connective tissue capsule
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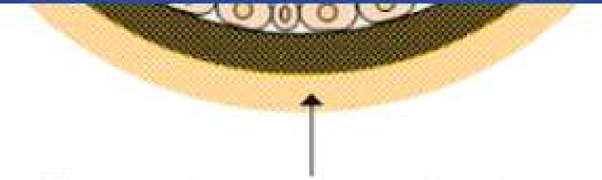

Estradiol, the predominant estrogen in the human body, is primarily derived from androgens. Androgens and progesterone are synthesized from cholesterol in the theca interna cells under the influence of luteinizing hormone (LH). Androgens released from the theca interna cells migrate into the nearby granulosa cells, which contain the enzyme aromatase. Aromatase converts the androgens into estradiol. This reaction is stimulated by follicle stimulating hormone (FSH).

(Choice B) The theca externa lies outside of the theca interna and does not participate in steroidogenesis. The theca externa is composed of a layer of smooth muscle and fibroblast cells. It serves as a connective tissue support structure for the follicle.

(Choice D) Oocytes do not make the aromatase enzyme needed for conversion of androgens to estradiol. All female oocytes are formed during embryogenesis and remain arrested in prophase I until ovulation occurs. At each ovulation, a single oocyte completes meiosis I. Meiosis II occurs after fertilization.

(Choice E) Leydig cells are found only in the male testes. They are analogous in location and function to the theca interna cells of the ovarian follicle. Leydig cells are stimulated by LH to secrete testosterone.

Educational Objective:

LH stimulates the theca interna cells of the ovarian follicle to produce androgens. Aromatase within the follicle's granulosa cells subsequently converts these androgens to estradiol under FSH stimulation. The theca externa cells serve as a connective tissue support structure for the follicle.

Physiology	Female Reproductive System & Breast	Infertility
Subject	System	Topic

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Item 5 of 40
Question Id: 18918
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A 54-year-old postmenopausal woman comes to the office due to increasing vaginal pressure for the past 3 months. The patient has had no vaginal bleeding or abnormal discharge. BMI is 18 kg/m^2. Vital signs are normal. On speculum examination, the anterior vaginal wall bulges with the Valsalva maneuver. On bimanual examination, the uterus is small and mobile. Which of the following is the most likely underlying cause of this patient's presentation?

○ A. Chronic endometriosis
○ B. Prior uterine artery ligation
○ C. Pudendal nerve injury
○ D. Uterine leiomyomas

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- ✗ ● A. Chronic endometriosis (6%)
- ○ B. Prior uterine artery ligation (22%)
- ✓ ○ C. Pudendal nerve injury (45%)
- ○ D. Uterine leiomyomas (25%)

Incorrect
Correct answer
C

45%
Answered correctly

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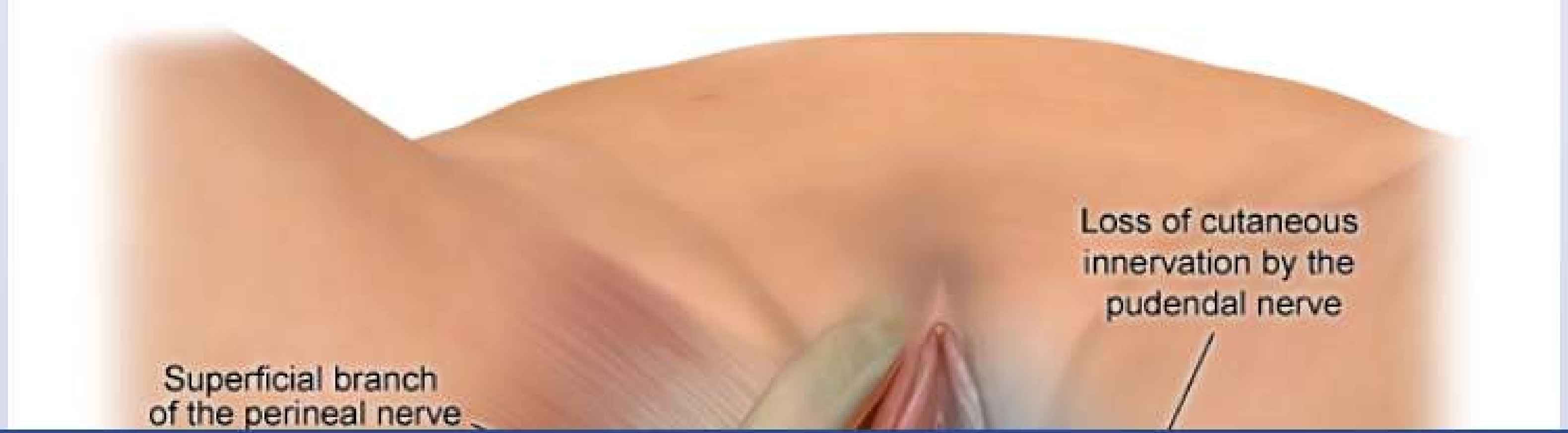
Explanation

Pudendal nerve injury



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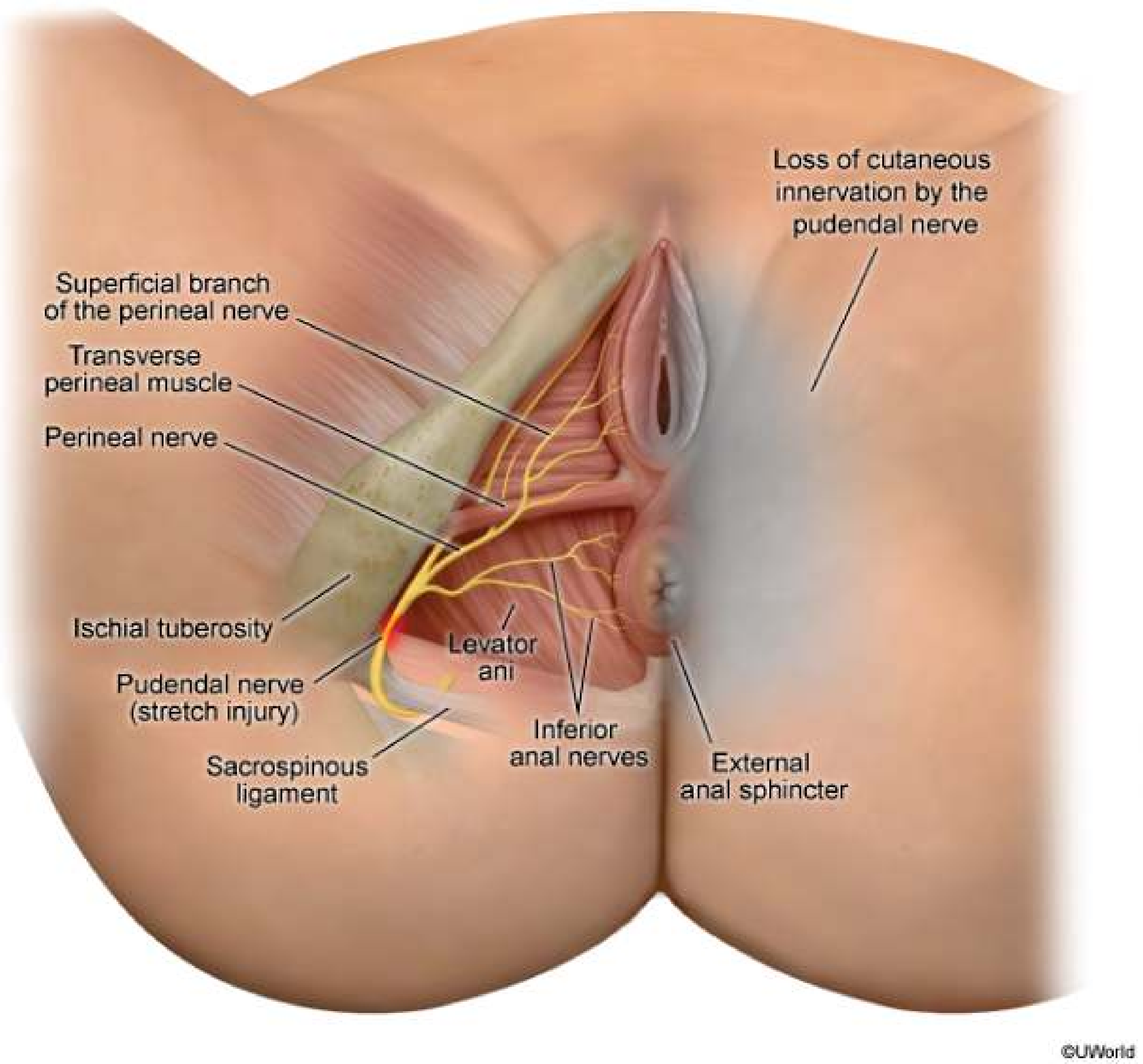
Pudendal nerve injury


Superficial branch
of the perineal nerve
Transverse
perineal muscle
Perineal nerve
Ischial tuberosity
Pudendal nerve
(stretch injury)
Sacrospinous
ligament
Levator
ani
Inferior
anal nerves
External
anal sphincter
Loss of cutaneous
innervation by the
pudendal nerve

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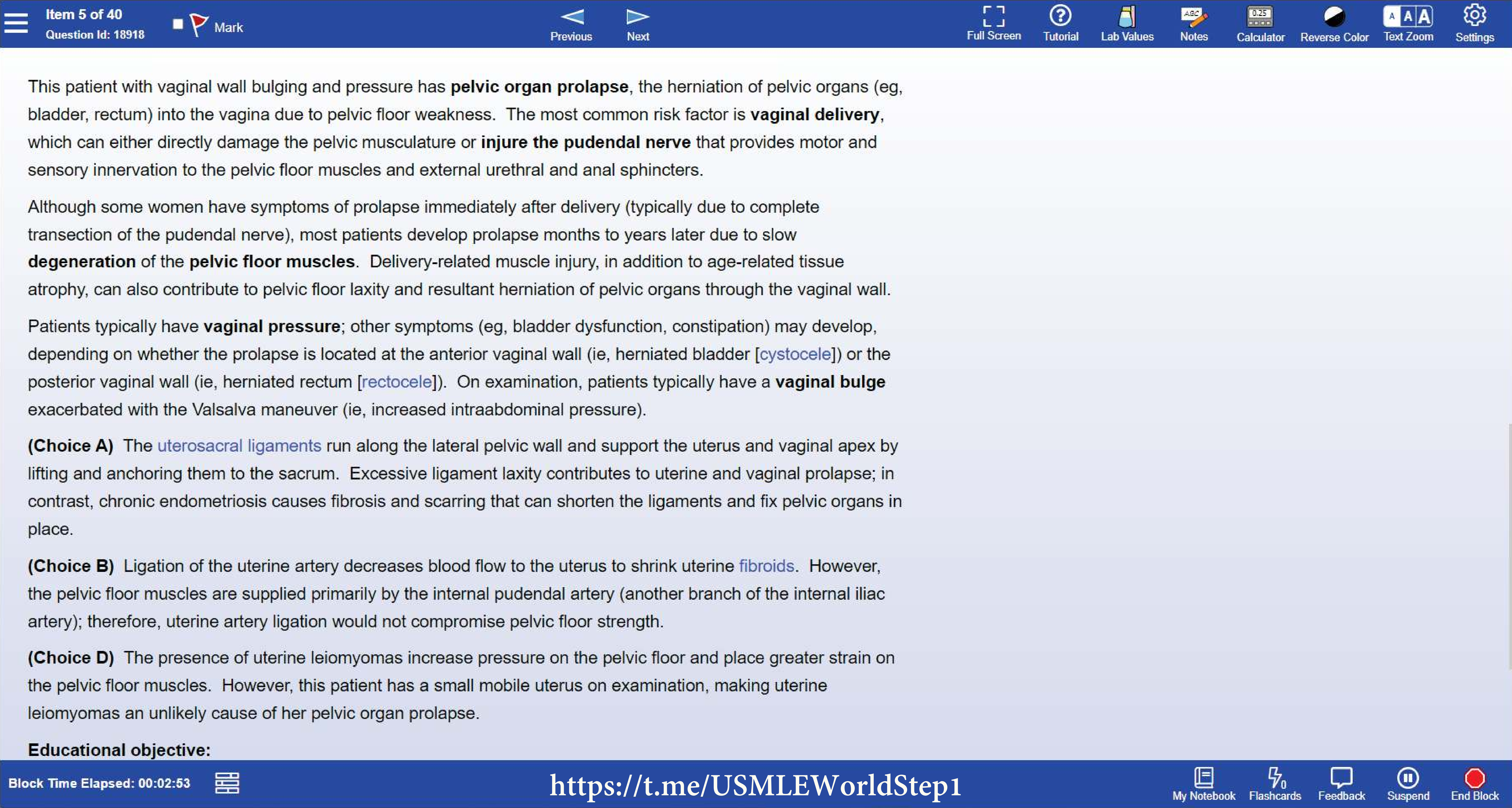
Ex

Superficial branch
of the perineal nerve



This patient with vaginal wall bulging and pressure has **pelvic organ prolapse**, the herniation of pelvic organs (eg, bladder, rectum) into the vagina due to pelvic floor weakness. The most common risk factor is **vaginal delivery**, which can either directly damage the pelvic musculature or **injure the pudendal nerve** that provides motor and sensory innervation to the pelvic floor muscles and external urethral and anal sphincters.

Although some women have symptoms of prolapse immediately after delivery (typically due to complete transection of the pudendal nerve), most patients develop prolapse months to years later due to slow **degeneration** of the **pelvic floor muscles**. Delivery-related muscle injury, in addition to age-related tissue atrophy, can also contribute to pelvic floor laxity and resultant herniation of pelvic organs through the vaginal wall.

Patients typically have **vaginal pressure**; other symptoms (eg, bladder dysfunction, constipation) may develop, depending on whether the prolapse is located at the anterior vaginal wall (ie, herniated bladder [cystocele]) or the posterior vaginal wall (ie, herniated rectum [rectocele]). On examination, patients typically have a **vaginal bulge** exacerbated with the Valsalva maneuver (ie, increased intraabdominal pressure).

(Choice A) The uterosacral ligaments run along the lateral pelvic wall and support the uterus and vaginal apex by lifting and anchoring them to the sacrum. Excessive ligament laxity contributes to uterine and vaginal prolapse; in contrast, chronic endometriosis causes fibrosis and scarring that can shorten the ligaments and fix pelvic organs in place.

(Choice B) Ligation of the uterine artery decreases blood flow to the uterus to shrink uterine fibroids. However, the pelvic floor muscles are supplied primarily by the internal pudendal artery (another branch of the internal iliac artery); therefore, uterine artery ligation would not compromise pelvic floor strength.

(Choice D) The presence of uterine leiomyomas increase pressure on the pelvic floor and place greater strain on the pelvic floor muscles. However, this patient has a small mobile uterus on examination, making uterine leiomyomas an unlikely cause of her pelvic organ prolapse.

Educational objective:

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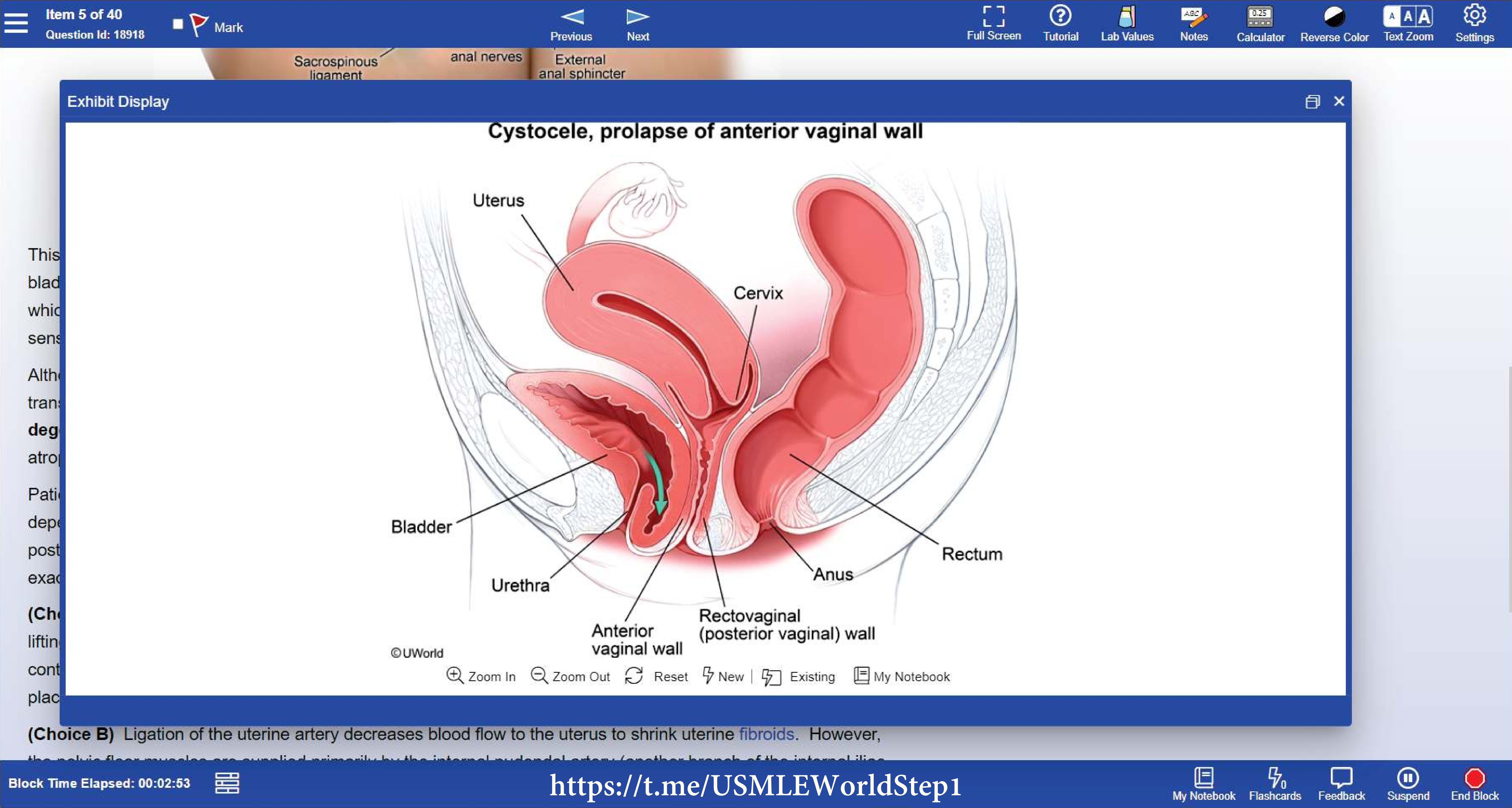
(Choice D) The presence of uterine leiomyomas increase pressure on the pelvic floor and place greater strain on the pelvic floor muscles. However, this patient has a small mobile uterus on examination, making uterine leiomyomas an unlikely cause of her pelvic organ prolapse.

Educational objective:

Pudendal nerve injury during vaginal delivery leads to gradual denervation and weakness of the pelvic floor muscles. In combination with age-related tissue atrophy, this injury contributes to pelvic organ prolapse (eg, cystocele).

References

- Pelvic organ prolapse.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Sacrospinous ligament
anal nerves
External anal sphincter
Exhibit Display
Uterus
Cervix
Bladder
Urethra
Anterior vaginal wall
Rectovaginal (posterior vaginal) wall
Anus
Rectum
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Cystocele, prolapse of anterior vaginal wall

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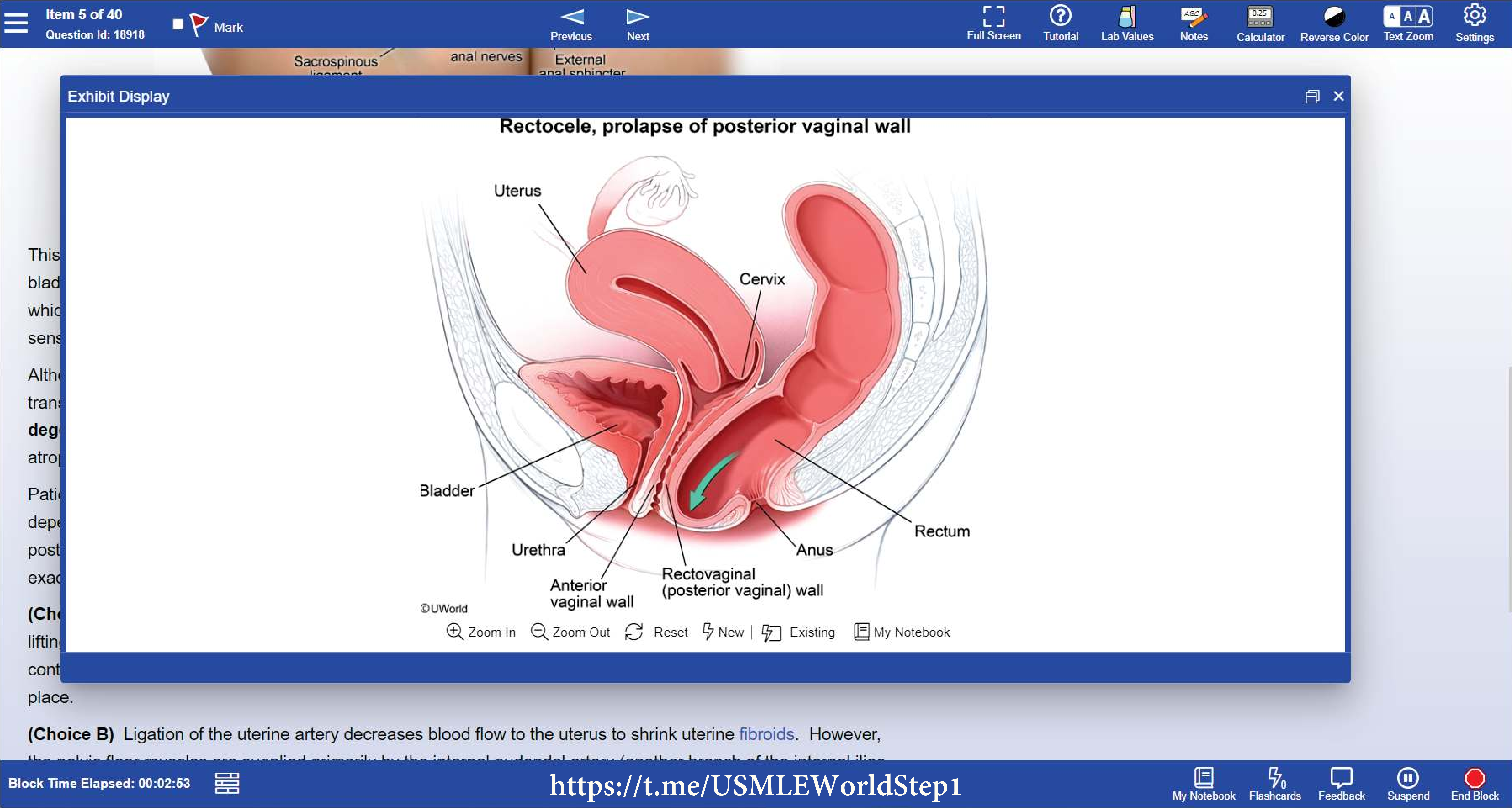
(Choice B) Ligation of the uterine artery decreases blood flow to the uterus to shrink uterine fibroids. However, the pelvic floor muscles are supplied primarily by the internal pudendal artery (another branch of the internal iliac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Rectocele, prolapse of posterior vaginal wall

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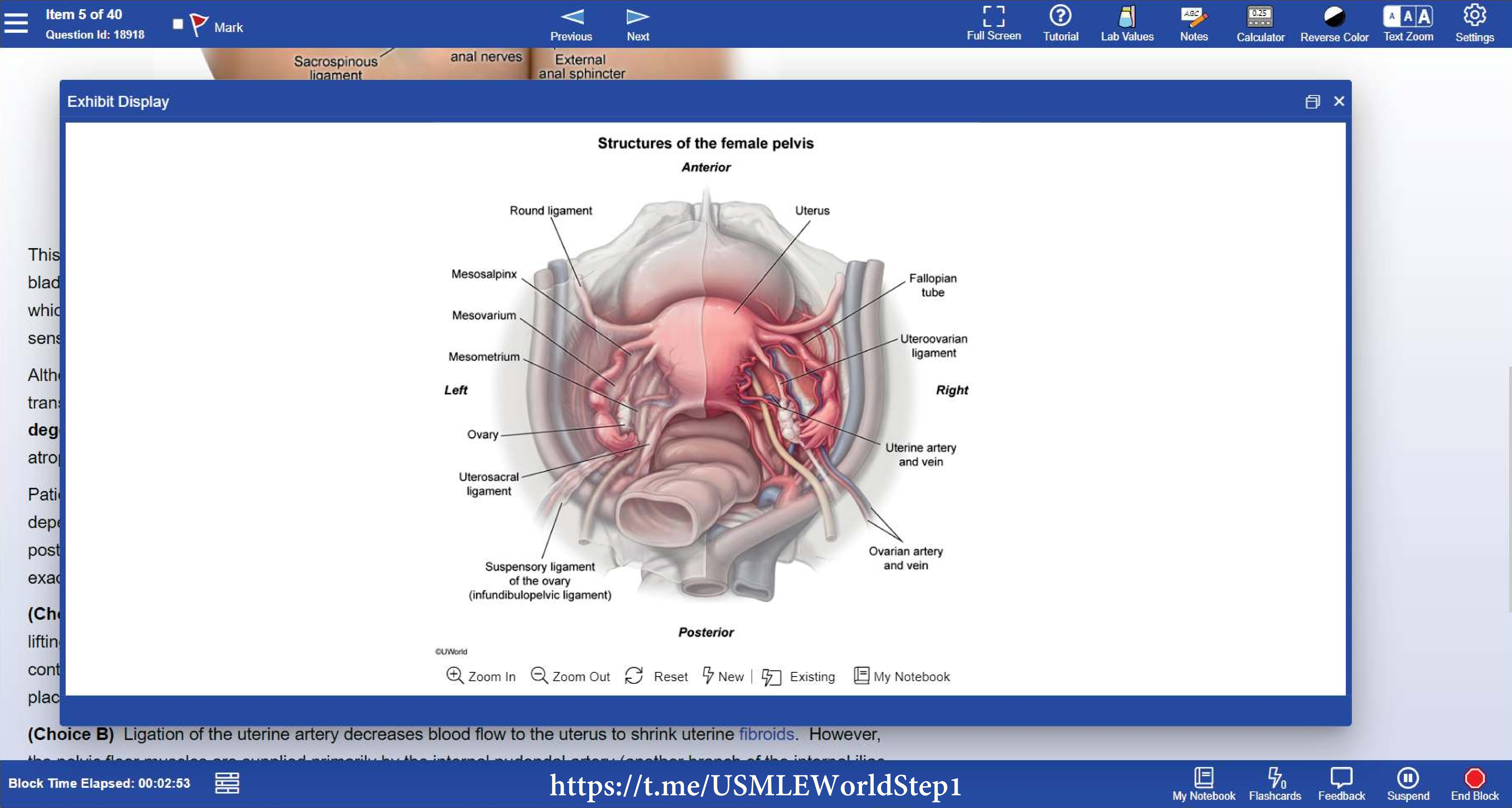
(Choice B) Ligation of the uterine artery decreases blood flow to the uterus to shrink uterine fibroids. However,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Sacrospinous ligament
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External anal sphincter
Exhibit Display
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Uterus
Mesosalpinx
Fallopian tube
Mesovarium
Uteroovarian ligament
Mesometrium
Left
Right
Ovary
Uterine artery and vein
Uterosacral ligament
Ovarian artery and vein
Suspensory ligament of the ovary (infundibulopelvic ligament)
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Structures of the female pelvis

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(Choice B) Ligation of the uterine artery decreases blood flow to the uterus to shrink uterine fibroids. However,

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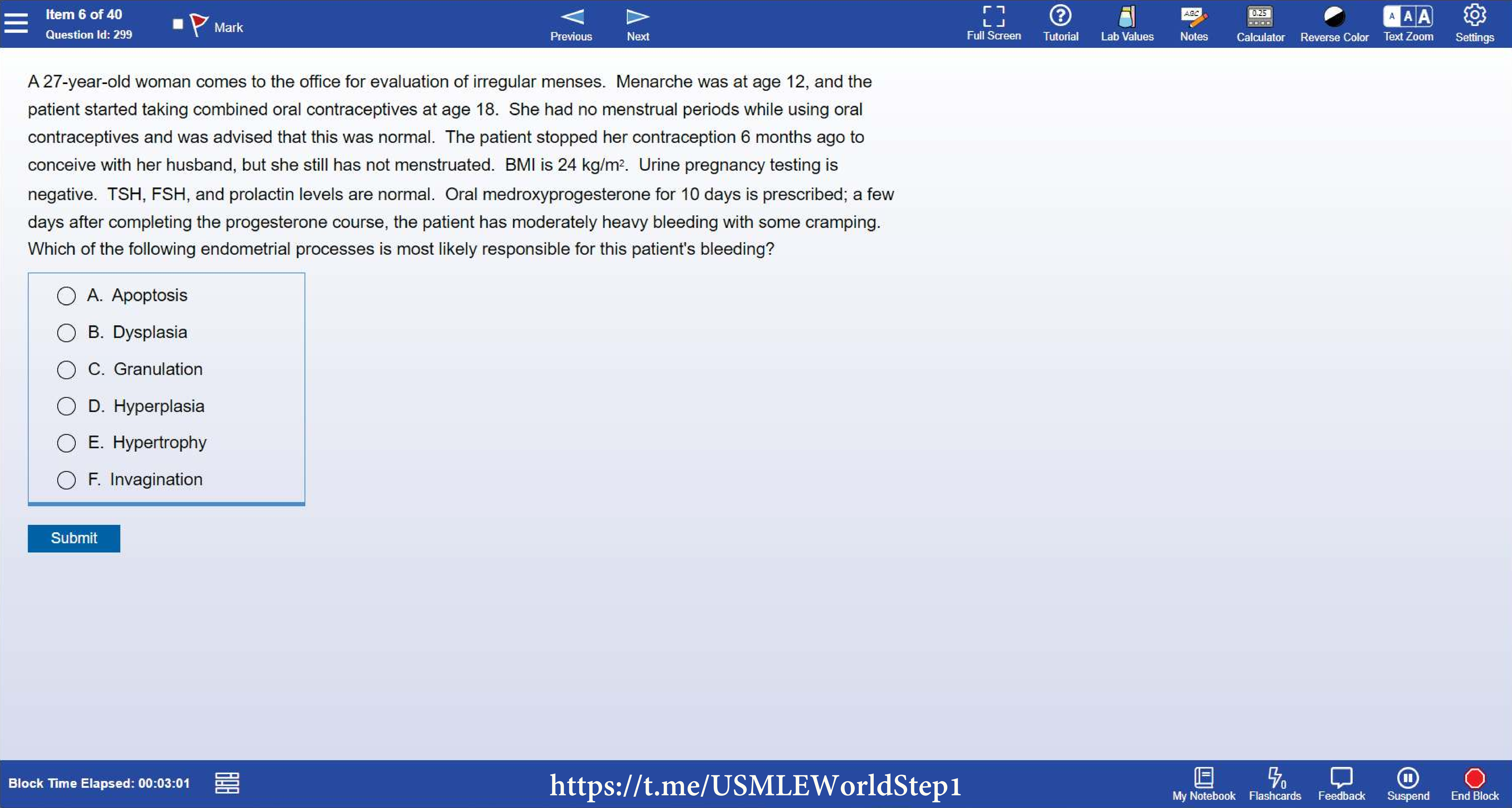
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Question Id: 299
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A 27-year-old woman comes to the office for evaluation of irregular menses. Menarche was at age 12, and the patient started taking combined oral contraceptives at age 18. She had no menstrual periods while using oral contraceptives and was advised that this was normal. The patient stopped her contraception 6 months ago to conceive with her husband, but she still has not menstruated. BMI is 24 kg/m^2. Urine pregnancy testing is negative. TSH, FSH, and prolactin levels are normal. Oral medroxyprogesterone for 10 days is prescribed; a few days after completing the progesterone course, the patient has moderately heavy bleeding with some cramping. Which of the following endometrial processes is most likely responsible for this patient's bleeding?

- ○ A. Apoptosis
- ○ B. Dysplasia
- ○ C. Granulation
- ○ D. Hyperplasia
- ○ E. Hypertrophy
- ○ F. Invagination

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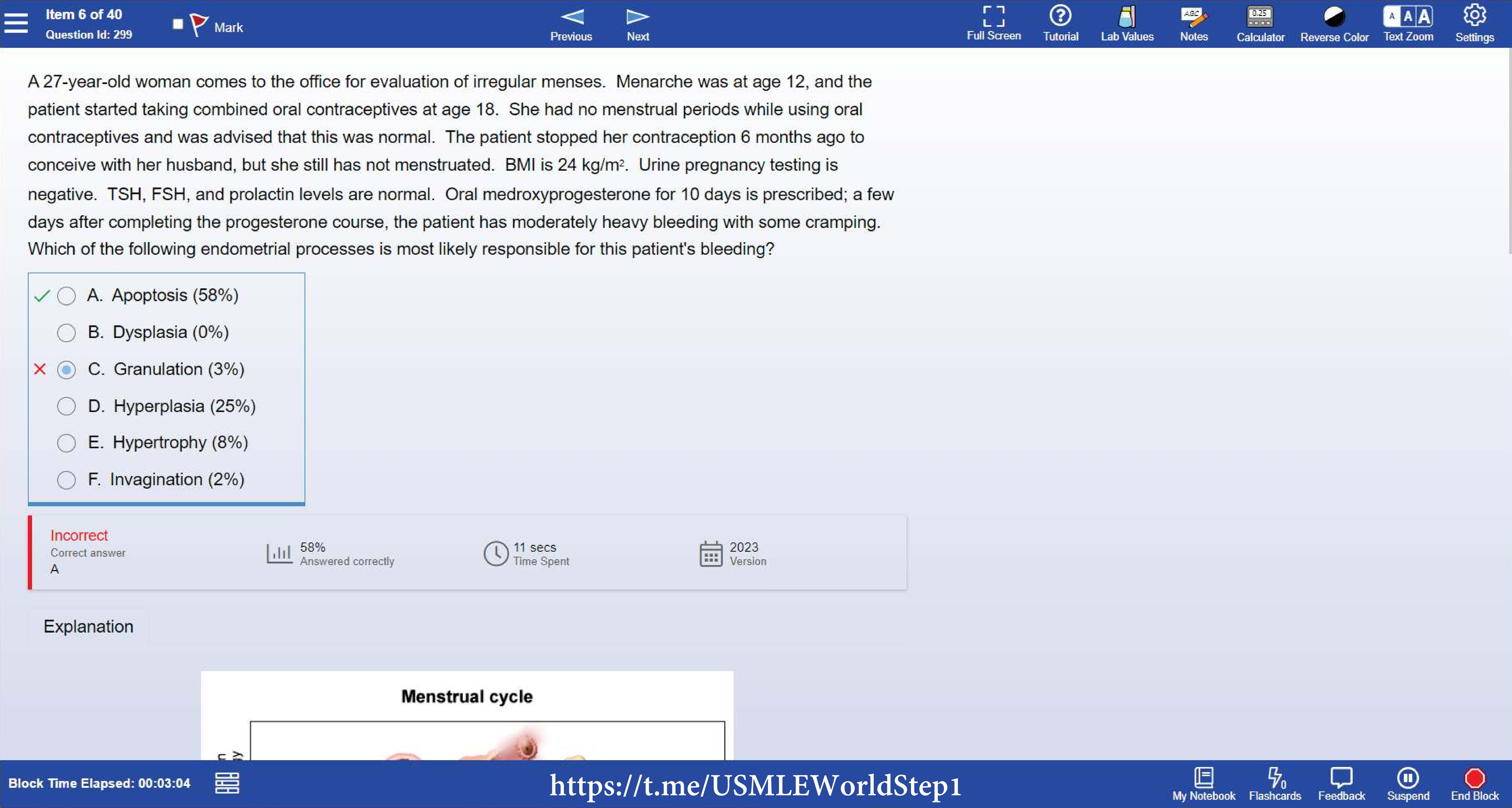
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Question Id: 299
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- ✓ ○ A. Apoptosis (58%)
- ○ B. Dysplasia (0%)
- ✗ ● C. Granulation (3%)
- ○ D. Hyperplasia (25%)
- ○ E. Hypertrophy (8%)
- ○ F. Invagination (2%)

Incorrect
Correct answer
A

58%
Answered correctly

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Explanation

Menstrual cycle

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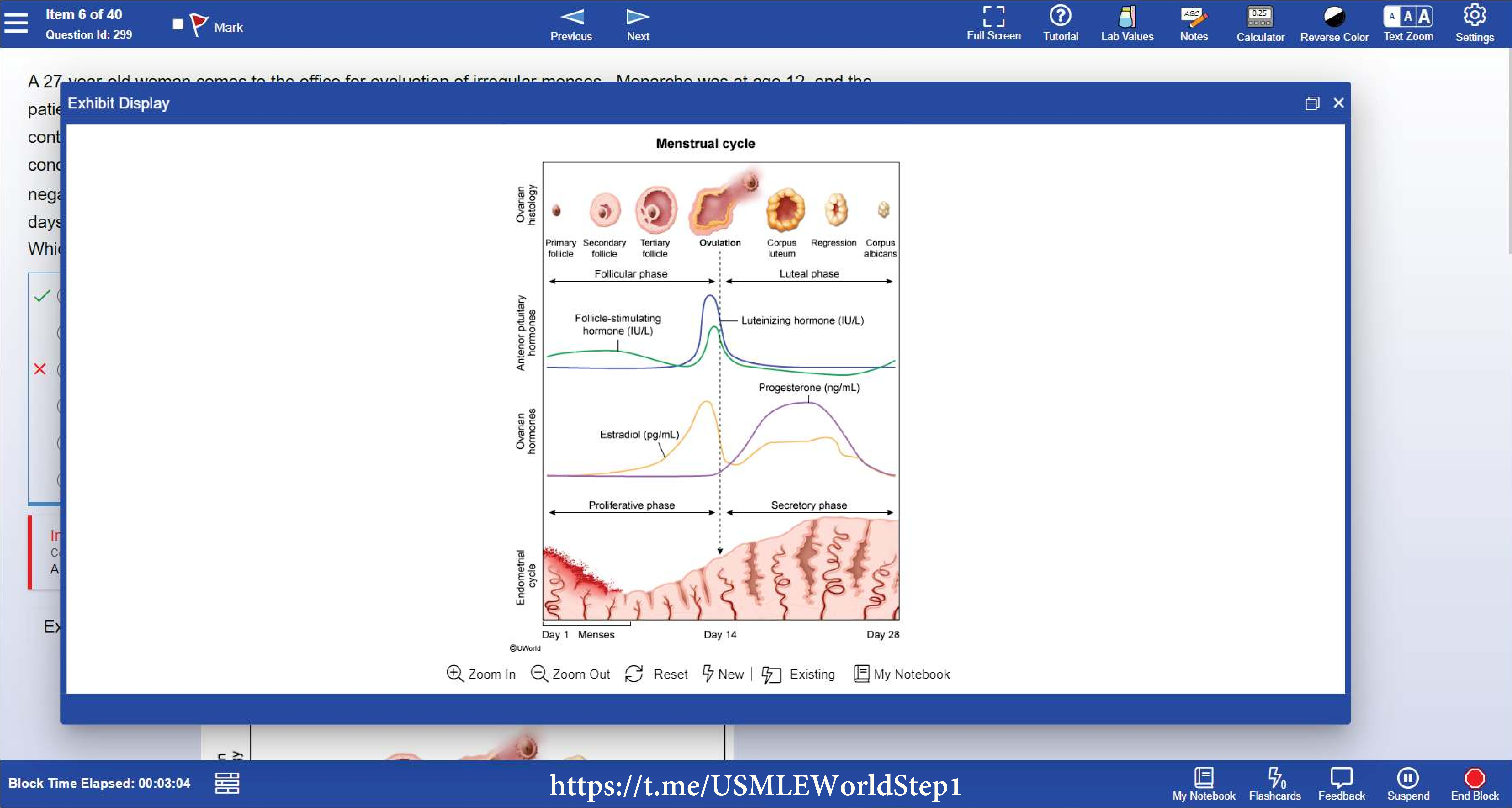

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Exhibit Display
Menstrual cycle
Ovarian histology
Primary follicle
Secondary follicle
Tertiary follicle
Ovulation
Corpus luteum
Regression
Corpus albicans
Follicular phase
Luteal phase
Anterior pituitary hormones
Follicle-stimulating hormone (IU/L)
Luteinizing hormone (IU/L)
Ovarian hormones
Progesterone (ng/mL)
Estradiol (pg/mL)
Proliferative phase
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Endometrial cycle
Day 1
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A 27 year-old woman comes to the office for evaluation of irregular menses. Menarche was at age 12, and the

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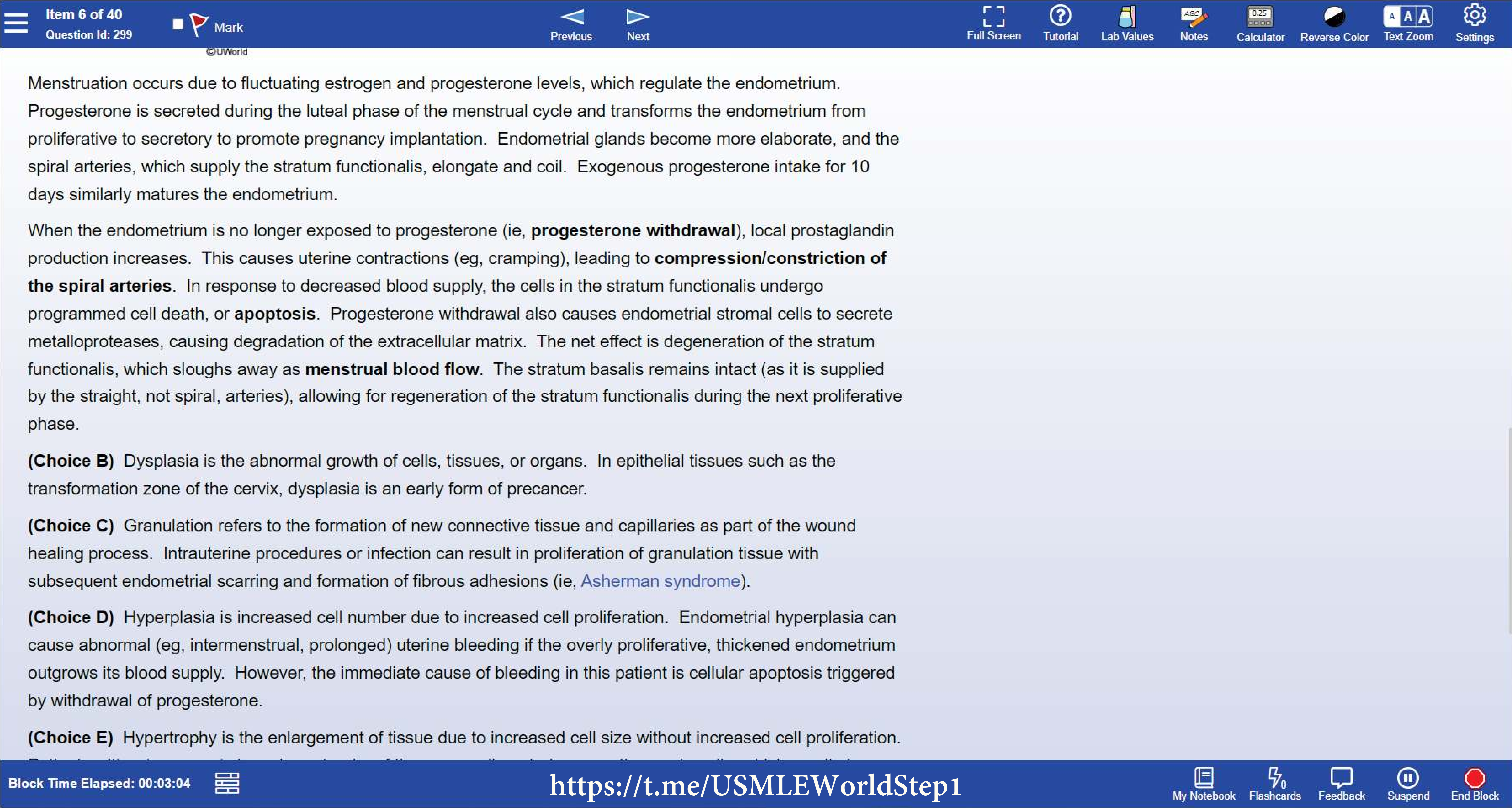

Menstruation occurs due to fluctuating estrogen and progesterone levels, which regulate the endometrium. Progesterone is secreted during the luteal phase of the menstrual cycle and transforms the endometrium from proliferative to secretory to promote pregnancy implantation. Endometrial glands become more elaborate, and the spiral arteries, which supply the stratum functionalis, elongate and coil. Exogenous progesterone intake for 10 days similarly matures the endometrium.

When the endometrium is no longer exposed to progesterone (ie, **progesterone withdrawal**), local prostaglandin production increases. This causes uterine contractions (eg, cramping), leading to **compression/constriction of the spiral arteries**. In response to decreased blood supply, the cells in the stratum functionalis undergo programmed cell death, or **apoptosis**. Progesterone withdrawal also causes endometrial stromal cells to secrete metalloproteases, causing degradation of the extracellular matrix. The net effect is degeneration of the stratum functionalis, which sloughs away as **menstrual blood flow**. The stratum basalis remains intact (as it is supplied by the straight, not spiral, arteries), allowing for regeneration of the stratum functionalis during the next proliferative phase.

(Choice B) Dysplasia is the abnormal growth of cells, tissues, or organs. In epithelial tissues such as the transformation zone of the cervix, dysplasia is an early form of precancer.

(Choice C) Granulation refers to the formation of new connective tissue and capillaries as part of the wound healing process. Intrauterine procedures or infection can result in proliferation of granulation tissue with subsequent endometrial scarring and formation of fibrous adhesions (ie, Asherman syndrome).

(Choice D) Hyperplasia is increased cell number due to increased cell proliferation. Endometrial hyperplasia can cause abnormal (eg, intermenstrual, prolonged) uterine bleeding if the overly proliferative, thickened endometrium outgrows its blood supply. However, the immediate cause of bleeding in this patient is cellular apoptosis triggered by withdrawal of progesterone.

(Choice E) Hypertrophy is the enlargement of tissue due to increased cell size without increased cell proliferation.

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(Choice E) Hypertrophy is the enlargement of tissue due to increased cell size without increased cell proliferation. Patients with adenomyosis have hypertrophy of the surrounding uterine smooth muscle cells, which results in a uniformly enlarged, globular uterus.

(Choice F) Invagination (inward folding) of epithelial cells occurs during embryonic development (gastrulation) to form structures such as the neural tube. It is not associated with menstruation.

Educational objective:

Progesterone is secreted during the luteal phase of the menstrual cycle and transforms the endometrium from proliferative to secretory. Progesterone withdrawal causes endometrial cells in the stratum functionalis to undergo apoptosis, resulting in menstrual bleeding.

When the endometrium is no longer exposed to progesterone (ie, **progesterone withdrawal**), local prostaglandin

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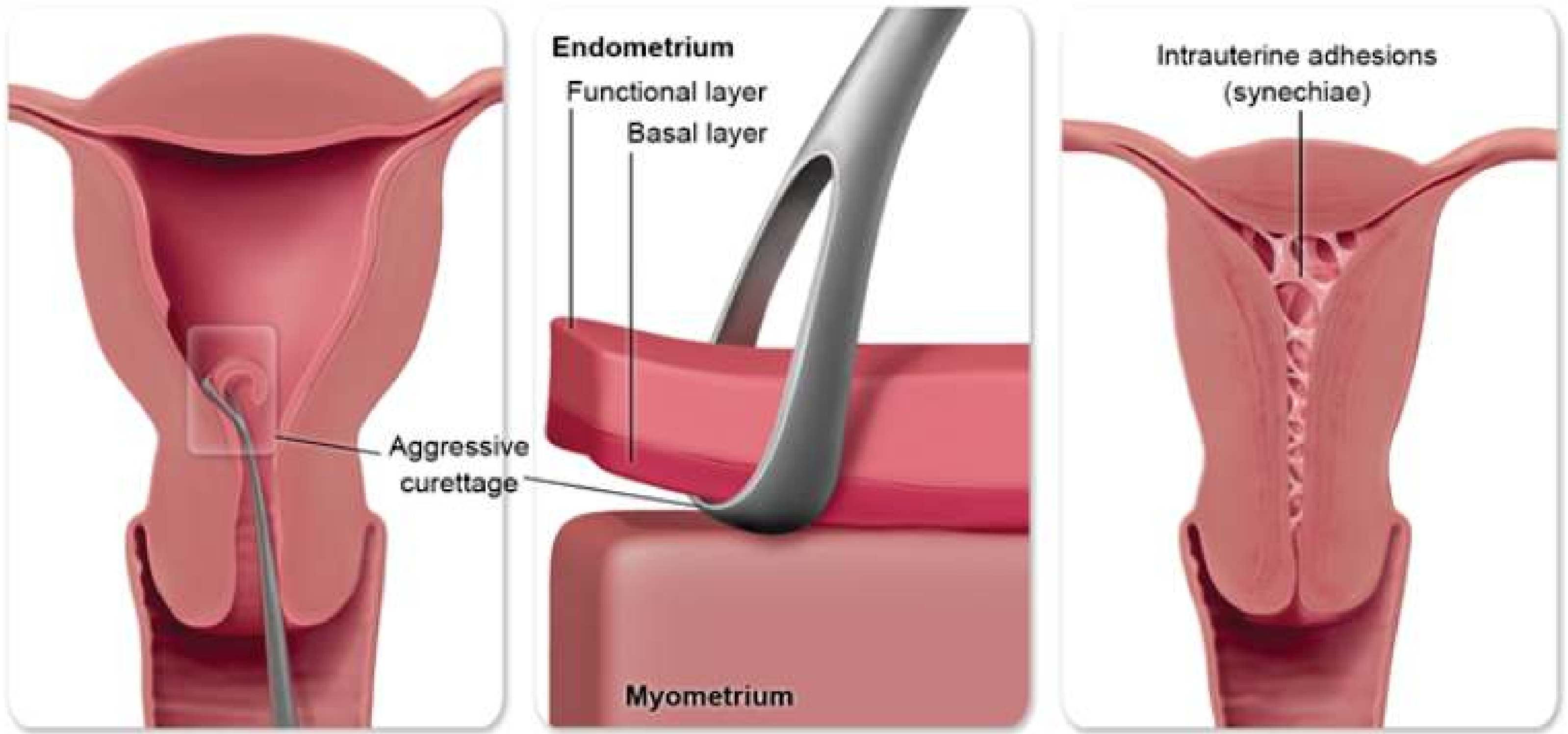
Asherman syndrome


Aggressive curettage
Endometrium
Functional layer
Basal layer
Myometrium
Intrauterine adhesions (synechiae)

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Educational objective:

Progesterone is secreted during the luteal phase of the menstrual cycle and transforms the endometrium from by the straight, not spiral, arteries), allowing for regeneration of the stratum functionalis during the next proliferative

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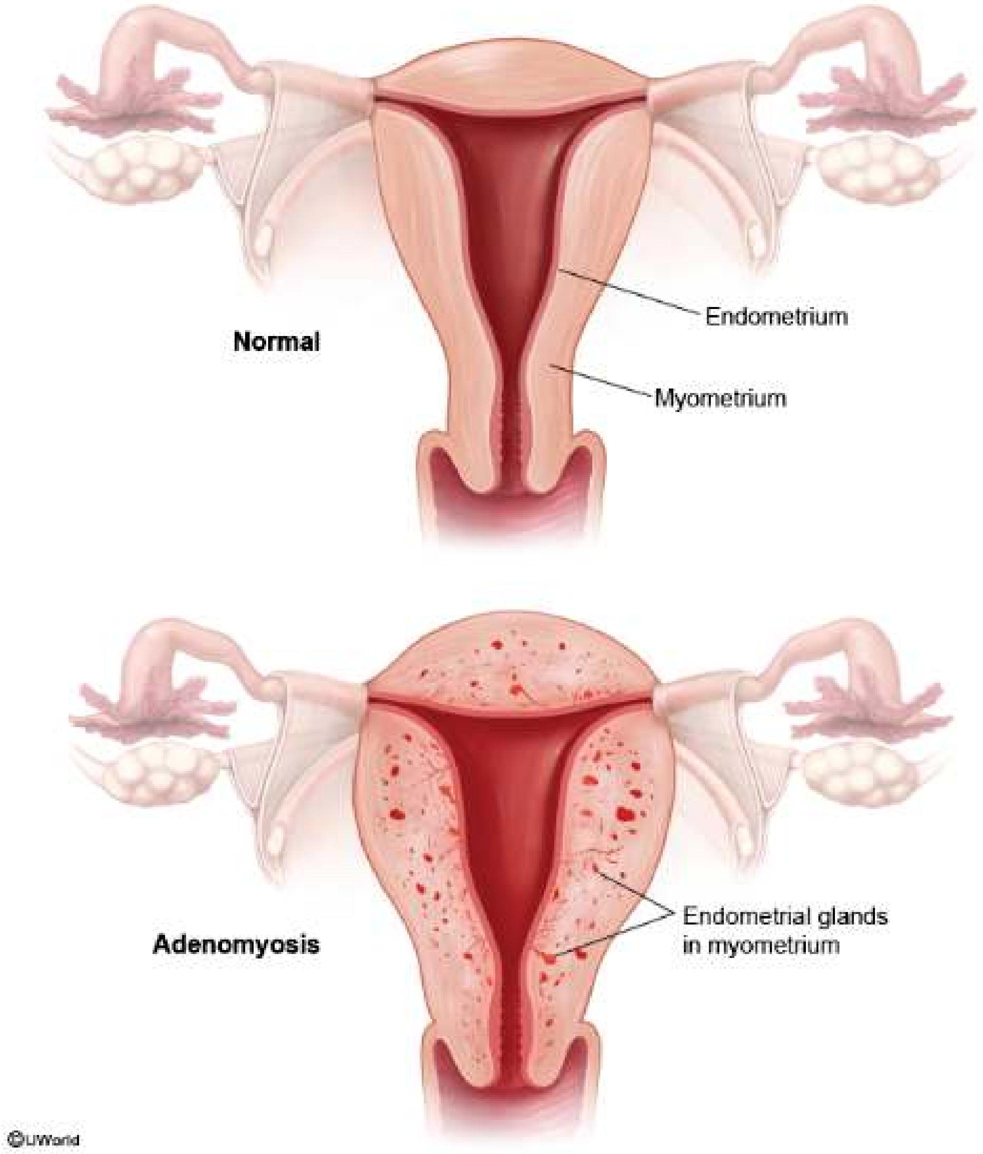
Endometrium
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Endometrial glands
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Refe

- Apoptosis in human endometrium and endometriosis.
- Regulation of human endometrial function: mechanisms relevant to uterine bleeding.

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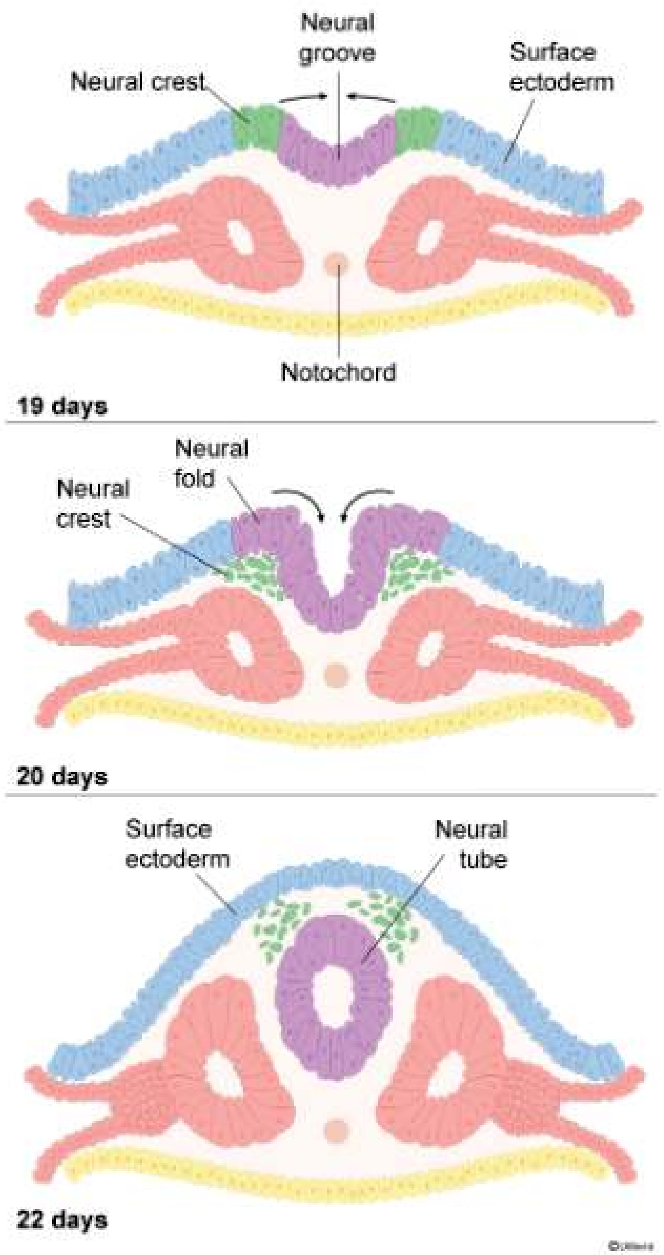
Neural tube formation


Neural groove
Neural crest
Surface ectoderm
Notochord
19 days
Neural fold
Neural crest
20 days
Surface ectoderm
Neural tube
22 days

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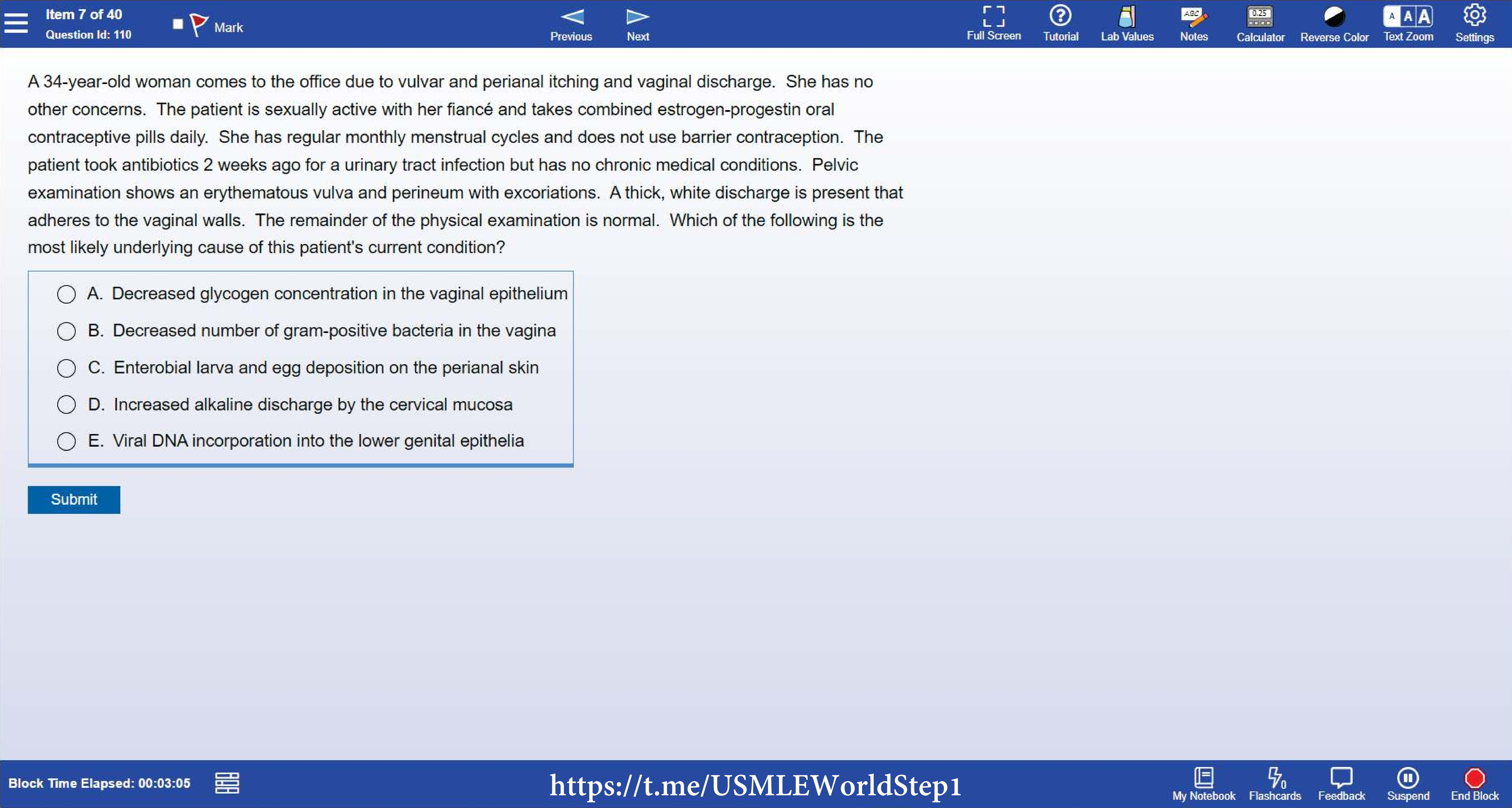
- A
- Regulation of human endometrial function: mechanisms relevant to uterine bleeding.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Item 7 of 40
Question Id: 110

A 34-year-old woman comes to the office due to vulvar and perianal itching and vaginal discharge. She has no other concerns. The patient is sexually active with her fiancé and takes combined estrogen-progestin oral contraceptive pills daily. She has regular monthly menstrual cycles and does not use barrier contraception. The patient took antibiotics 2 weeks ago for a urinary tract infection but has no chronic medical conditions. Pelvic examination shows an erythematous vulva and perineum with excoriations. A thick, white discharge is present that adheres to the vaginal walls. The remainder of the physical examination is normal. Which of the following is the most likely underlying cause of this patient's current condition?

- ○ A. Decreased glycogen concentration in the vaginal epithelium
- ○ B. Decreased number of gram-positive bacteria in the vagina
- ○ C. Enterobial larva and egg deposition on the perianal skin
- ○ D. Increased alkaline discharge by the cervical mucosa
- ○ E. Viral DNA incorporation into the lower genital epithelia

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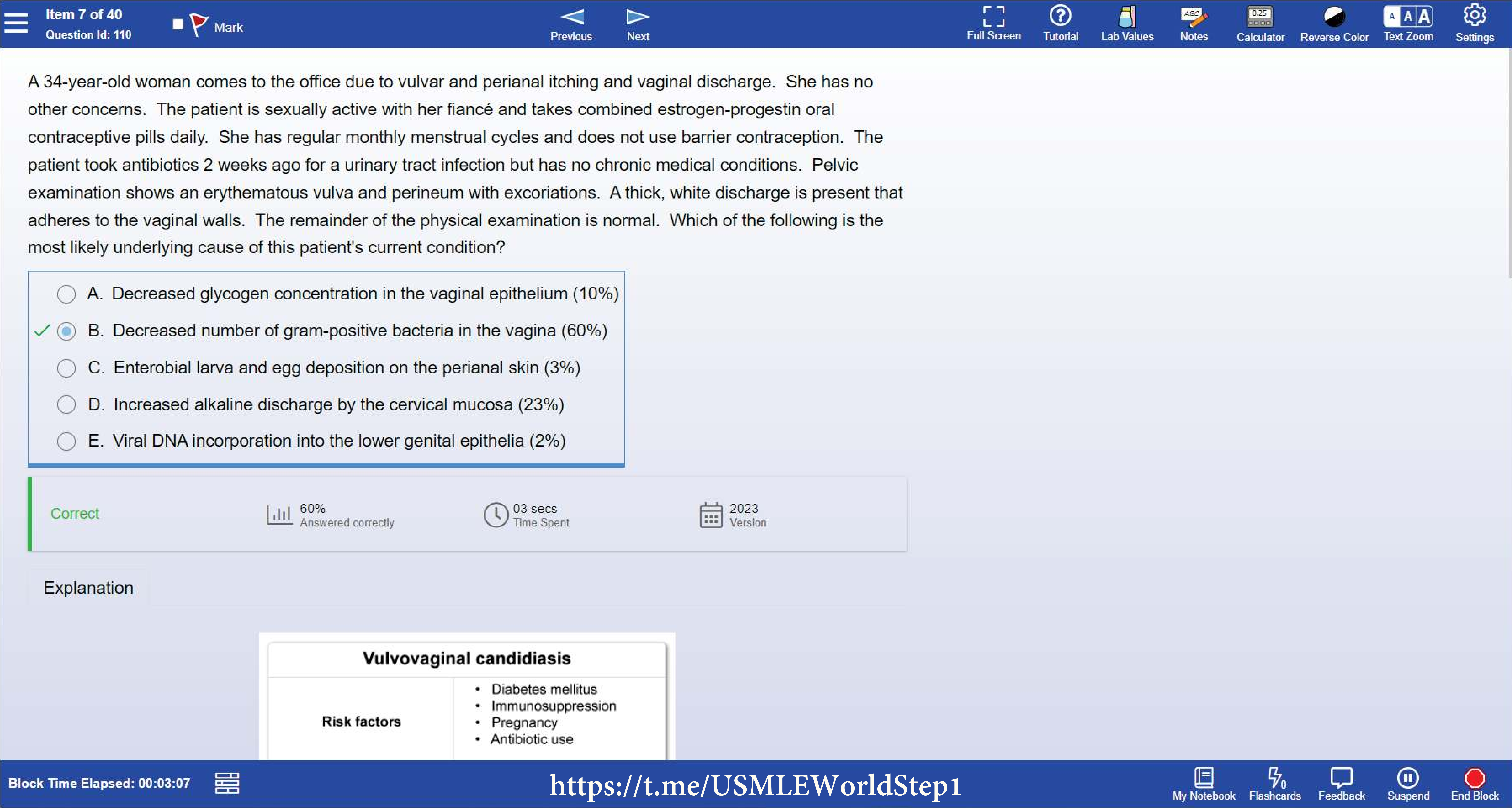
Item 7 of 40
Question Id: 110
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○ A. Decreased glycogen concentration in the vaginal epithelium (10%)

✓ ● B. Decreased number of gram-positive bacteria in the vagina (60%)

○ C. Enterobial larva and egg deposition on the perianal skin (3%)

○ D. Increased alkaline discharge by the cervical mucosa (23%)

○ E. Viral DNA incorporation into the lower genital epithelia (2%)

Correct

60%
Answered correctly

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Explanation

Vulvovaginal candidiasis

Risk factors	• Diabetes mellitus • Immunosuppression • Pregnancy • Antibiotic use

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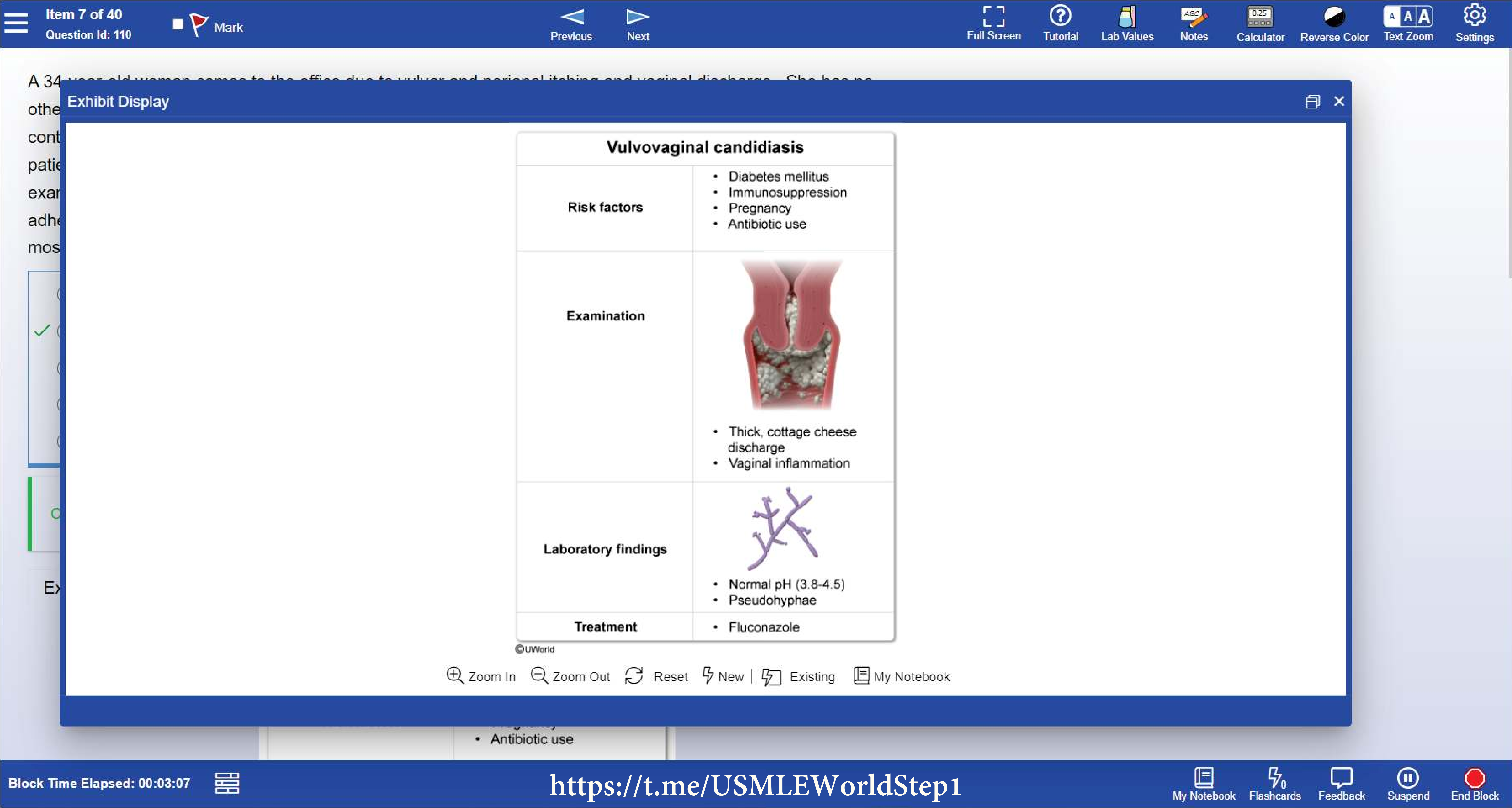
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Vulvovaginal candidiasis

Risk factors	• Diabetes mellitus • Immunosuppression • Pregnancy • Antibiotic use
Examination	• Thick, cottage cheese discharge • Vaginal inflammation
Laboratory findings	• Normal pH (3.8-4.5) • Pseudohyphae
Treatment	• Fluconazole

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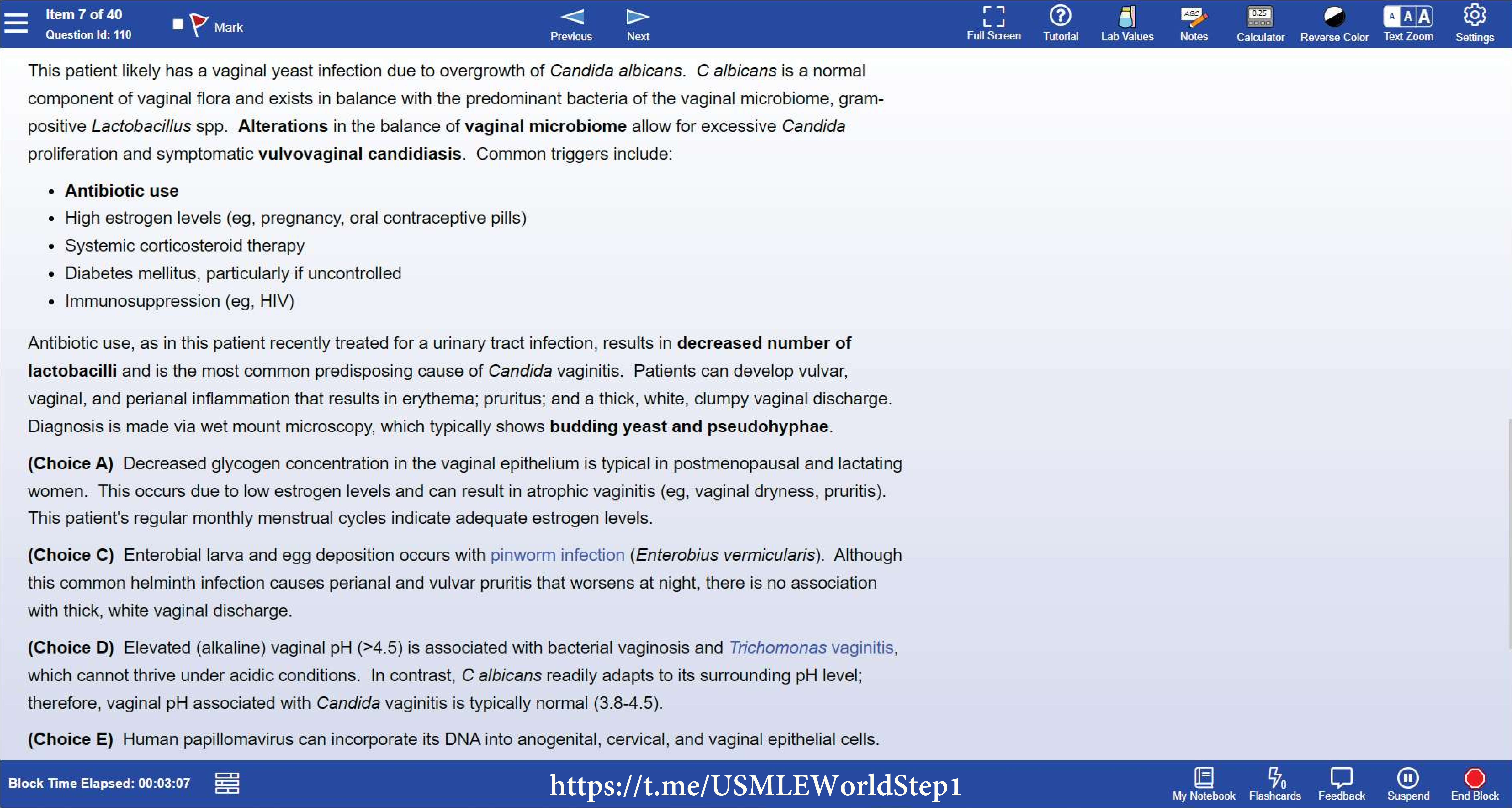


This patient likely has a vaginal yeast infection due to overgrowth of *Candida albicans*. *C albicans* is a normal component of vaginal flora and exists in balance with the predominant bacteria of the vaginal microbiome, gram-positive *Lactobacillus* spp. **Alterations** in the balance of **vaginal microbiome** allow for excessive *Candida* proliferation and symptomatic **vulvovaginal candidiasis**. Common triggers include:

- **Antibiotic use**
- High estrogen levels (eg, pregnancy, oral contraceptive pills)
- Systemic corticosteroid therapy
- Diabetes mellitus, particularly if uncontrolled
- Immunosuppression (eg, HIV)

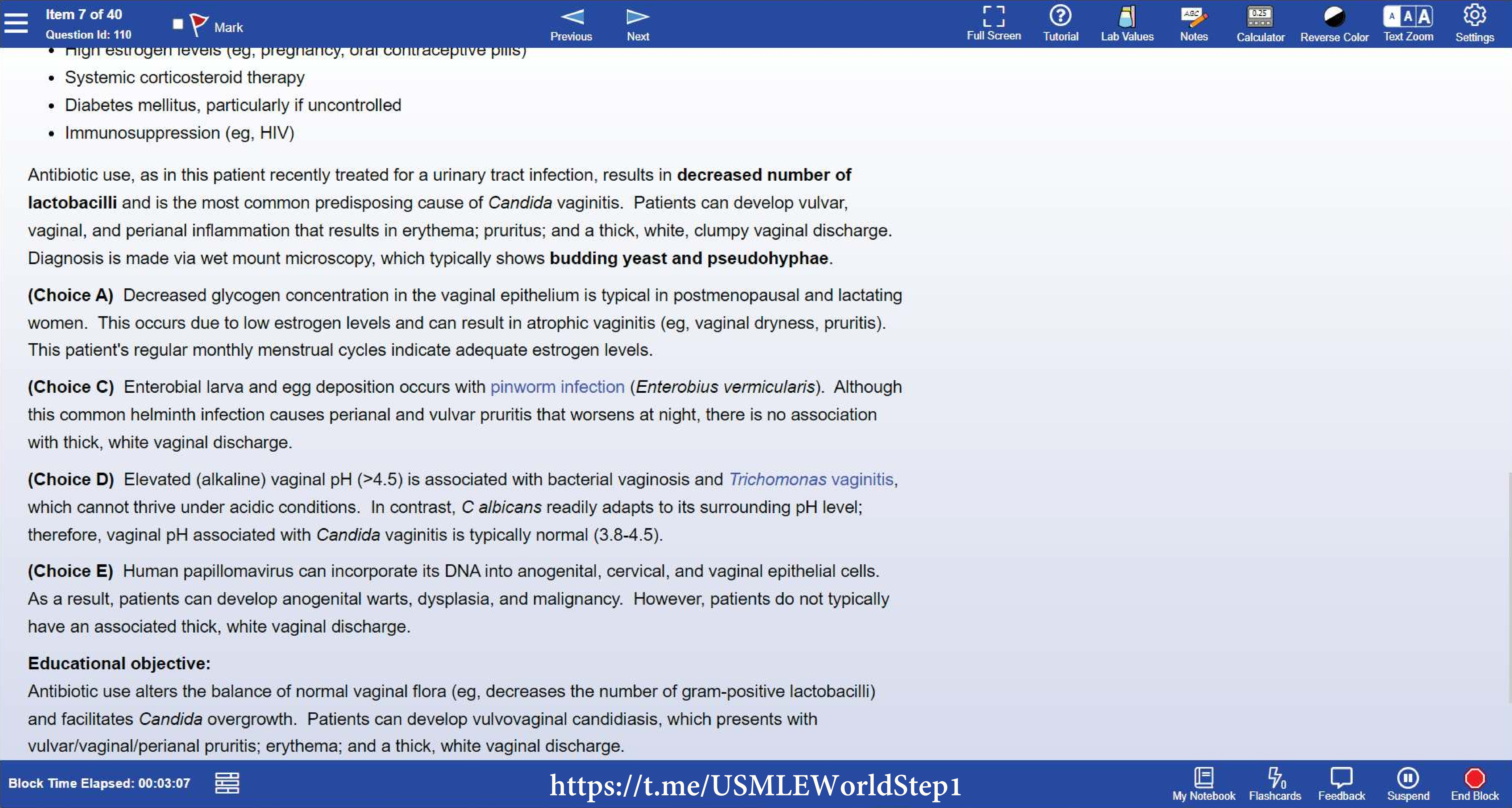
Antibiotic use, as in this patient recently treated for a urinary tract infection, results in **decreased number of lactobacilli** and is the most common predisposing cause of *Candida* vaginitis. Patients can develop vulvar, vaginal, and perianal inflammation that results in erythema; pruritus; and a thick, white, clumpy vaginal discharge. Diagnosis is made via wet mount microscopy, which typically shows **budding yeast and pseudohyphae**.

(Choice A) Decreased glycogen concentration in the vaginal epithelium is typical in postmenopausal and lactating women. This occurs due to low estrogen levels and can result in atrophic vaginitis (eg, vaginal dryness, pruritis). This patient's regular monthly menstrual cycles indicate adequate estrogen levels.

(Choice C) Enterobial larva and egg deposition occurs with pinworm infection (*Enterobius vermicularis*). Although this common helminth infection causes perianal and vulvar pruritis that worsens at night, there is no association with thick, white vaginal discharge.

(Choice D) Elevated (alkaline) vaginal pH (>4.5) is associated with bacterial vaginosis and *Trichomonas* vaginitis, which cannot thrive under acidic conditions. In contrast, *C albicans* readily adapts to its surrounding pH level; therefore, vaginal pH associated with *Candida* vaginitis is typically normal (3.8-4.5).

(Choice E) Human papillomavirus can incorporate its DNA into anogenital, cervical, and vaginal epithelial cells.



- High estrogen levels (eg, pregnancy, oral contraceptive pills)
- Systemic corticosteroid therapy
- Diabetes mellitus, particularly if uncontrolled
- Immunosuppression (eg, HIV)

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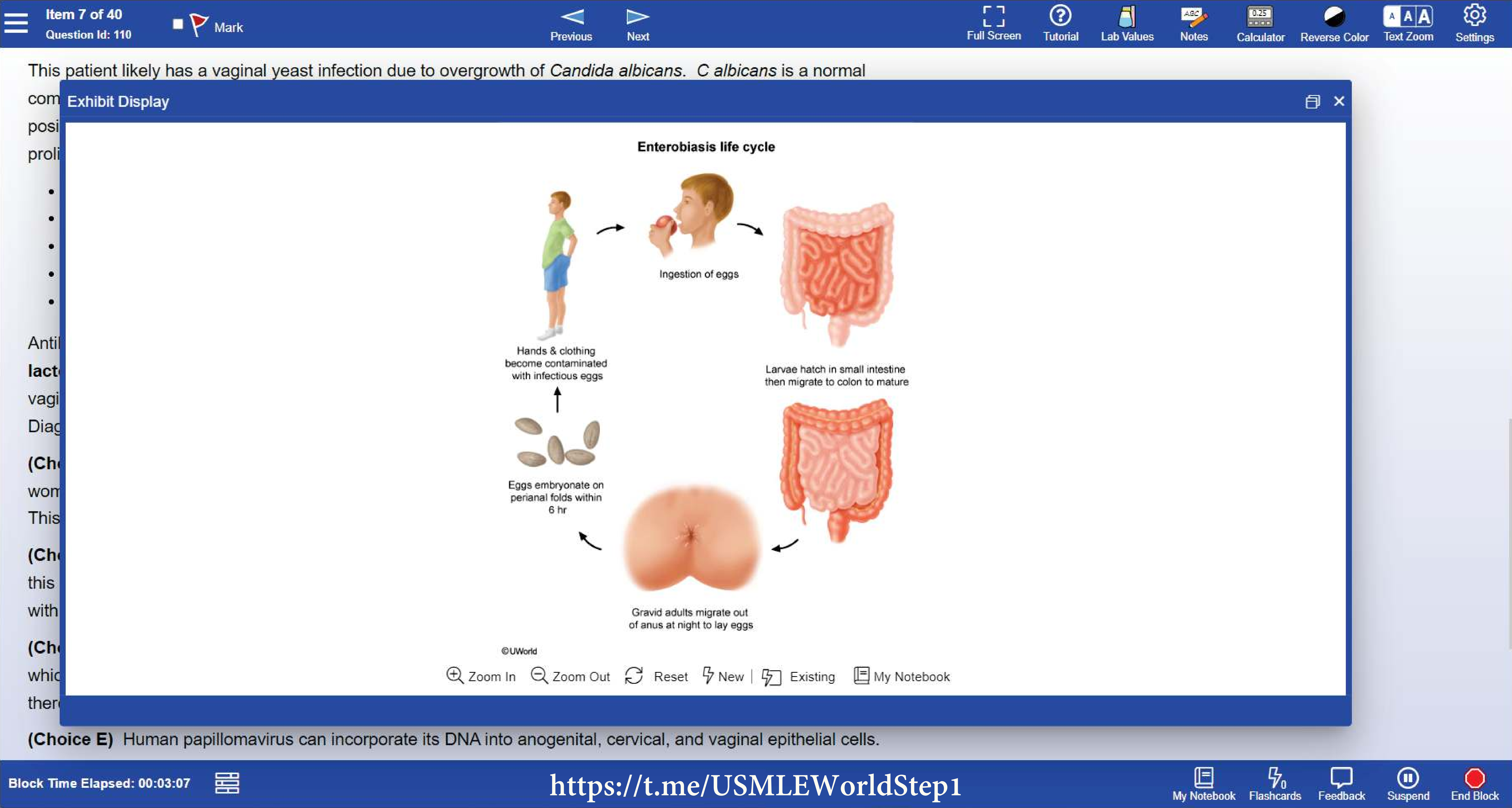
(Choice E) Human papillomavirus can incorporate its DNA into anogenital, cervical, and vaginal epithelial cells. As a result, patients can develop anogenital warts, dysplasia, and malignancy. However, patients do not typically have an associated thick, white vaginal discharge.

Educational objective:

Antibiotic use alters the balance of normal vaginal flora (eg, decreases the number of gram-positive lactobacilli) and facilitates *Candida* overgrowth. Patients can develop vulvovaginal candidiasis, which presents with vulvar/vaginal/perianal pruritis; erythema; and a thick, white vaginal discharge.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This patient likely has a vaginal yeast infection due to overgrowth of *Candida albicans*. *C albicans* is a normal

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Enterobiasis life cycle

Ingestion of eggs
Larvae hatch in small intestine then migrate to colon to mature
Gravid adults migrate out of anus at night to lay eggs
Eggs embryonate on perianal folds within 6 hr
Hands & clothing become contaminated with infectious eggs
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(Choice E) Human papillomavirus can incorporate its DNA into anogenital, cervical, and vaginal epithelial cells.

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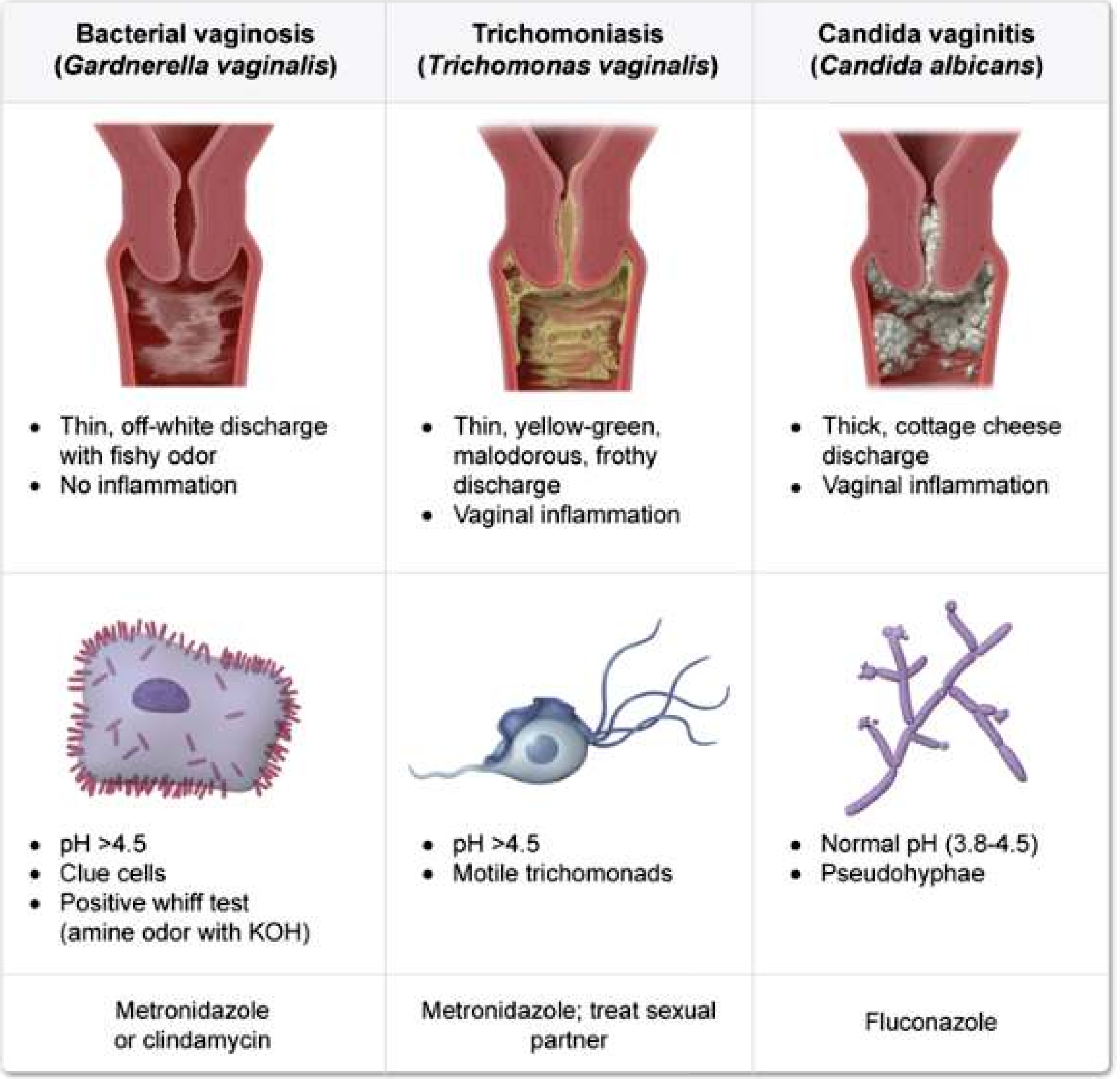
Differential diagnosis of vaginitis



Bacterial vaginosis (*Gardnerella vaginalis*)	**Trichomoniasis (*Trichomonas vaginalis*)**	**Candida vaginitis (*Candida albicans*)**
- Thin, off-white discharge with fishy odor - No inflammation	- Thin, yellow-green, malodorous, frothy discharge - Vaginal inflammation	- Thick, cottage cheese discharge - Vaginal inflammation
- pH >4.5 - Clue cells - Positive whiff test (amine odor with KOH)	- pH >4.5 - Motile trichomonads	- Normal pH (3.8-4.5) - Pseudohyphae
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

KOH = potassium hydroxide.

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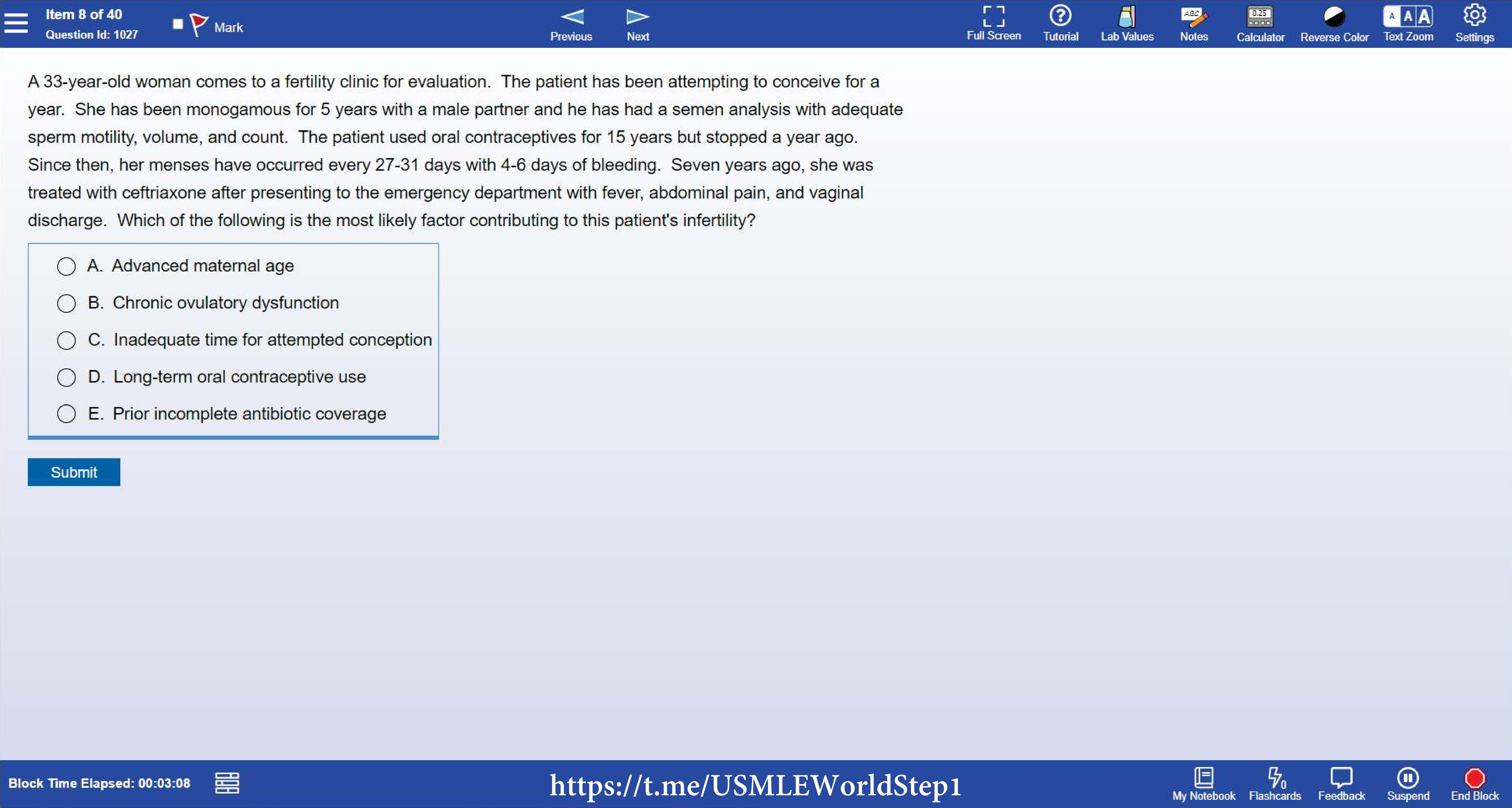
(Choice E) Human papillomavirus can incorporate its DNA into anogenital, cervical, and vaginal epithelial cells.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A 33-year-old woman comes to a fertility clinic for evaluation. The patient has been attempting to conceive for a year. She has been monogamous for 5 years with a male partner and he has had a semen analysis with adequate sperm motility, volume, and count. The patient used oral contraceptives for 15 years but stopped a year ago. Since then, her menses have occurred every 27-31 days with 4-6 days of bleeding. Seven years ago, she was treated with ceftriaxone after presenting to the emergency department with fever, abdominal pain, and vaginal discharge. Which of the following is the most likely factor contributing to this patient's infertility?

○ A. Advanced maternal age
○ B. Chronic ovulatory dysfunction
○ C. Inadequate time for attempted conception
○ D. Long-term oral contraceptive use
○ E. Prior incomplete antibiotic coverage

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○ A. Advanced maternal age (3%)

✗ ● B. Chronic ovulatory dysfunction (6%)

○ C. Inadequate time for attempted conception (5%)

○ D. Long-term oral contraceptive use (7%)

✓ ○ E. Prior incomplete antibiotic coverage (77%)

Incorrect
Correct answer
E

77%
Answered correctly

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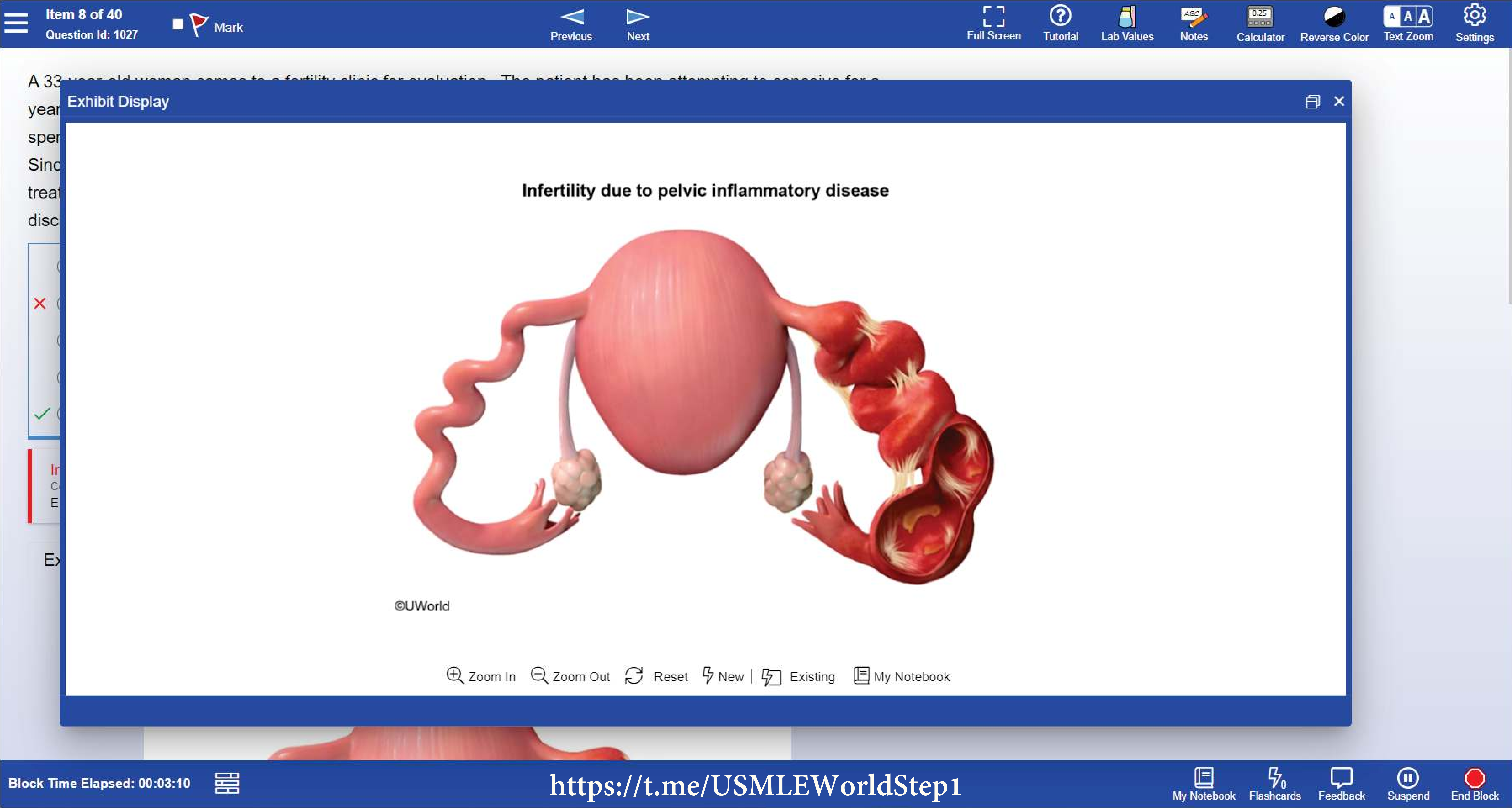
Explanation

Infertility due to pelvic inflammatory disease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Infertility due to pelvic inflammatory disease

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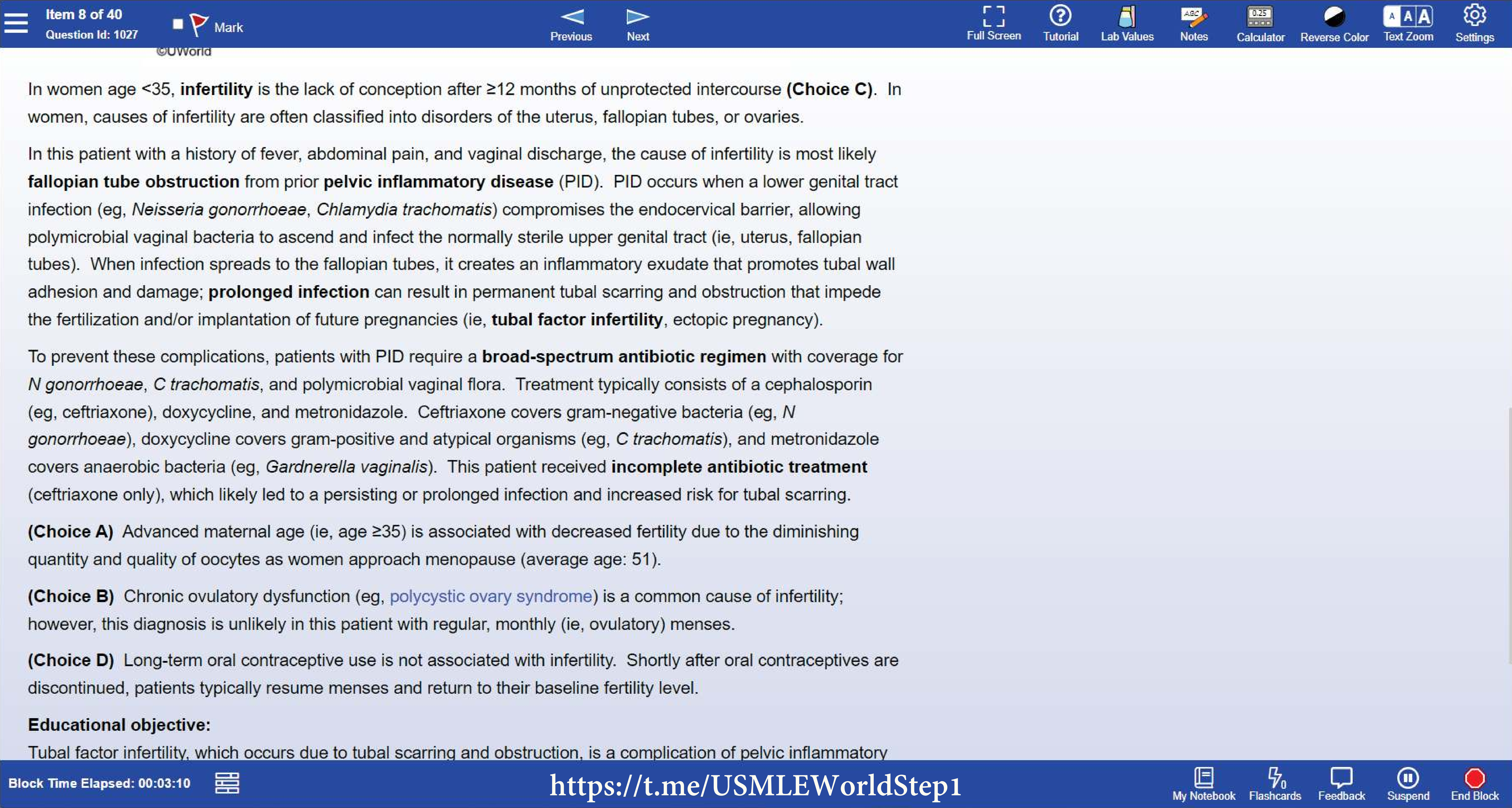

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In women age <35, **infertility** is the lack of conception after ≥12 months of unprotected intercourse **(Choice C)**. In women, causes of infertility are often classified into disorders of the uterus, fallopian tubes, or ovaries.

In this patient with a history of fever, abdominal pain, and vaginal discharge, the cause of infertility is most likely **fallopian tube obstruction** from prior **pelvic inflammatory disease** (PID). PID occurs when a lower genital tract infection (eg, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*) compromises the endocervical barrier, allowing polymicrobial vaginal bacteria to ascend and infect the normally sterile upper genital tract (ie, uterus, fallopian tubes). When infection spreads to the fallopian tubes, it creates an inflammatory exudate that promotes tubal wall adhesion and damage; **prolonged infection** can result in permanent tubal scarring and obstruction that impede the fertilization and/or implantation of future pregnancies (ie, **tubal factor infertility**, ectopic pregnancy).

To prevent these complications, patients with PID require a **broad-spectrum antibiotic regimen** with coverage for *N gonorrhoeae*, *C trachomatis*, and polymicrobial vaginal flora. Treatment typically consists of a cephalosporin (eg, ceftriaxone), doxycycline, and metronidazole. Ceftriaxone covers gram-negative bacteria (eg, *N gonorrhoeae*), doxycycline covers gram-positive and atypical organisms (eg, *C trachomatis*), and metronidazole covers anaerobic bacteria (eg, *Gardnerella vaginalis*). This patient received **incomplete antibiotic treatment** (ceftriaxone only), which likely led to a persisting or prolonged infection and increased risk for tubal scarring.

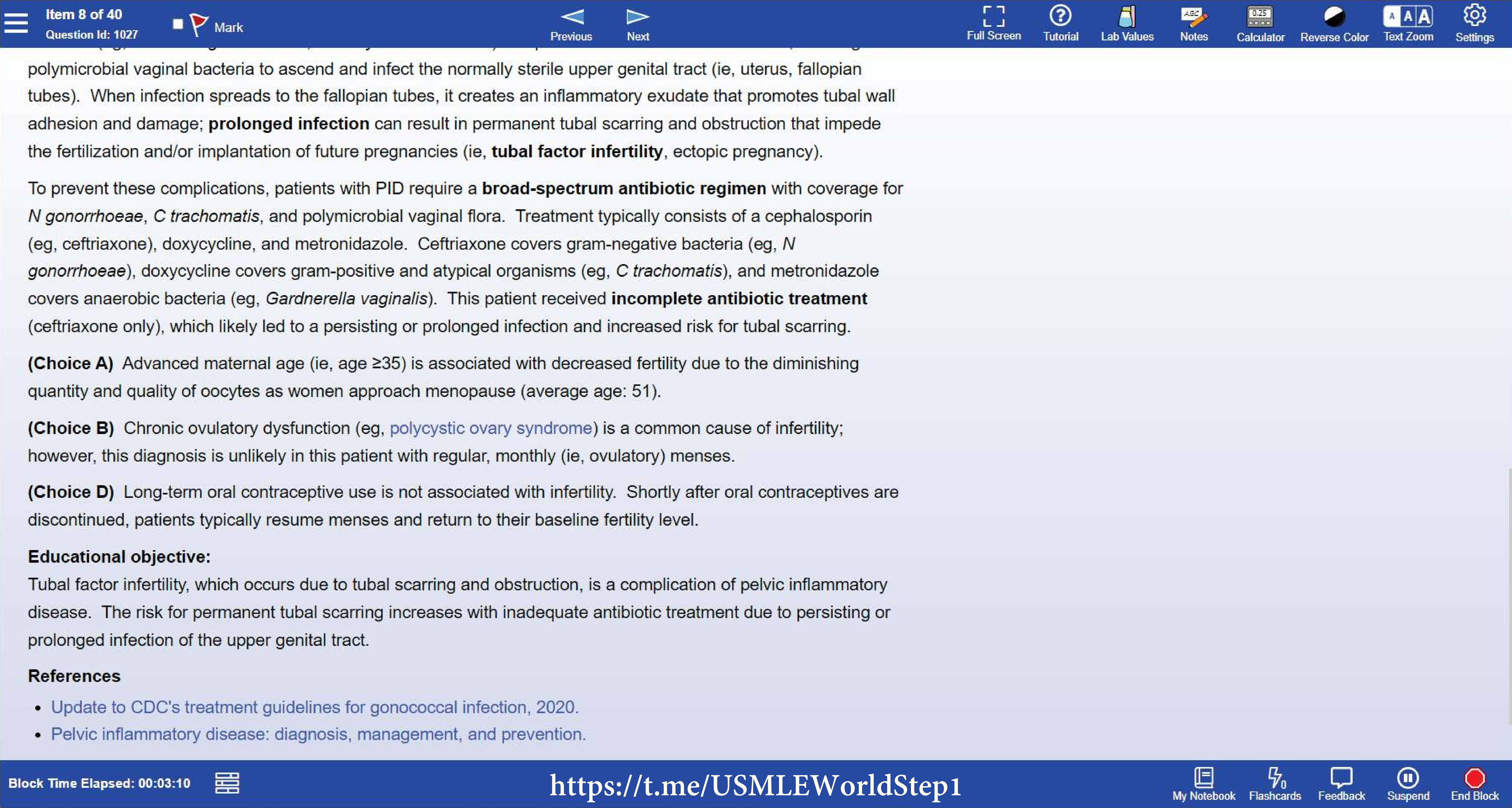
(Choice A) Advanced maternal age (ie, age ≥35) is associated with decreased fertility due to the diminishing quantity and quality of oocytes as women approach menopause (average age: 51).

(Choice B) Chronic ovulatory dysfunction (eg, polycystic ovary syndrome) is a common cause of infertility; however, this diagnosis is unlikely in this patient with regular, monthly (ie, ovulatory) menses.

(Choice D) Long-term oral contraceptive use is not associated with infertility. Shortly after oral contraceptives are discontinued, patients typically resume menses and return to their baseline fertility level.

Educational objective:

Tubal factor infertility, which occurs due to tubal scarring and obstruction, is a complication of pelvic inflammatory



polymicrobial vaginal bacteria to ascend and infect the normally sterile upper genital tract (ie, uterus, fallopian tubes). When infection spreads to the fallopian tubes, it creates an inflammatory exudate that promotes tubal wall adhesion and damage; **prolonged infection** can result in permanent tubal scarring and obstruction that impede the fertilization and/or implantation of future pregnancies (ie, **tubal factor infertility**, ectopic pregnancy).

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Educational objective:

Tubal factor infertility, which occurs due to tubal scarring and obstruction, is a complication of pelvic inflammatory disease. The risk for permanent tubal scarring increases with inadequate antibiotic treatment due to persisting or prolonged infection of the upper genital tract.

References

- Update to CDC's treatment guidelines for gonococcal infection, 2020.
- Pelvic inflammatory disease: diagnosis, management, and prevention.

In this patient with a history of fever, abdominal pain, and vaginal discharge, the cause of infertility is most likely

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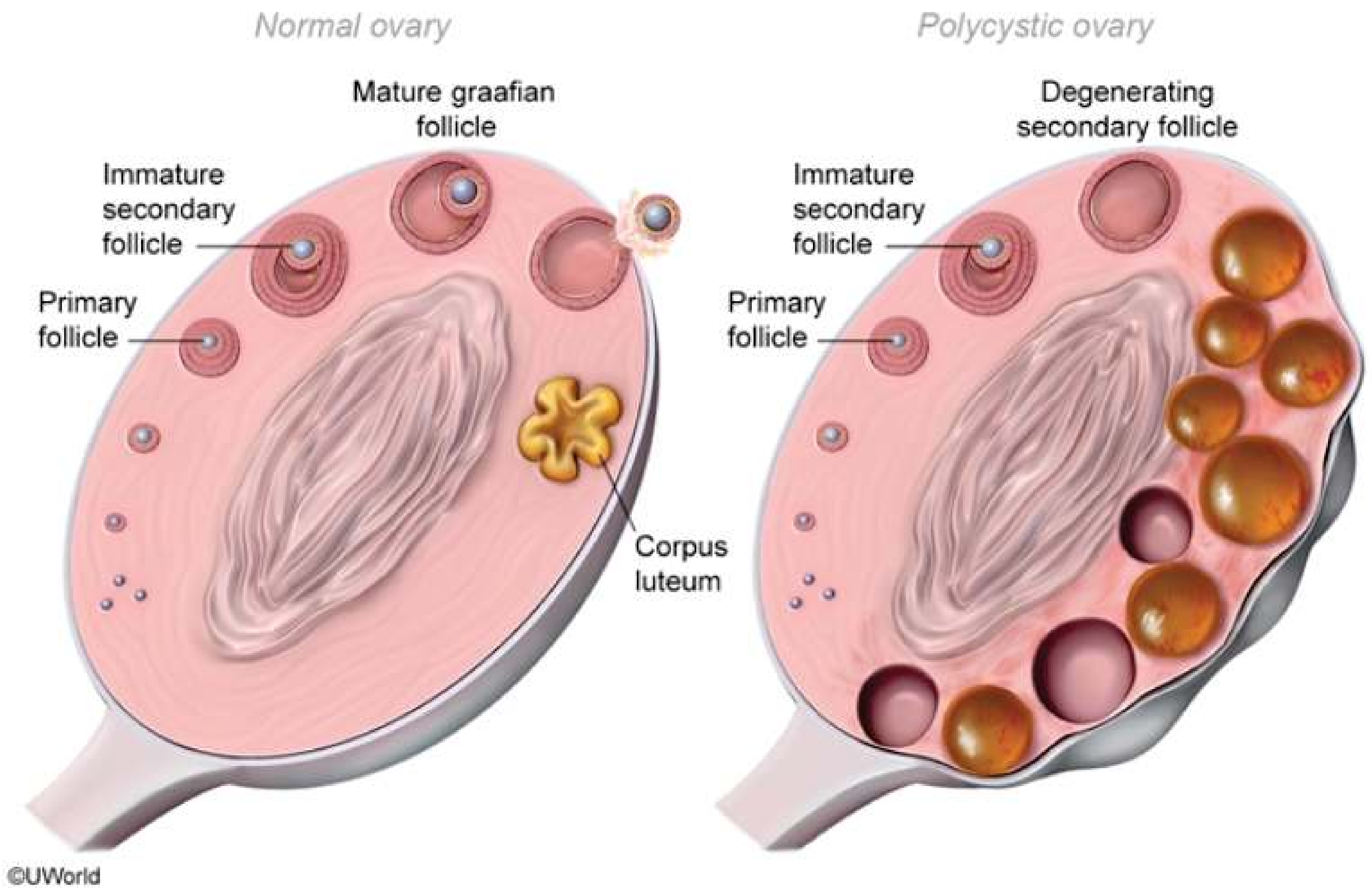
Polycystic ovary syndrome


Normal ovary
Polycystic ovary
Mature graafian follicle
Immature secondary follicle
Primary follicle
Corpus luteum
Degenerating secondary follicle
Immature secondary follicle
Primary follicle

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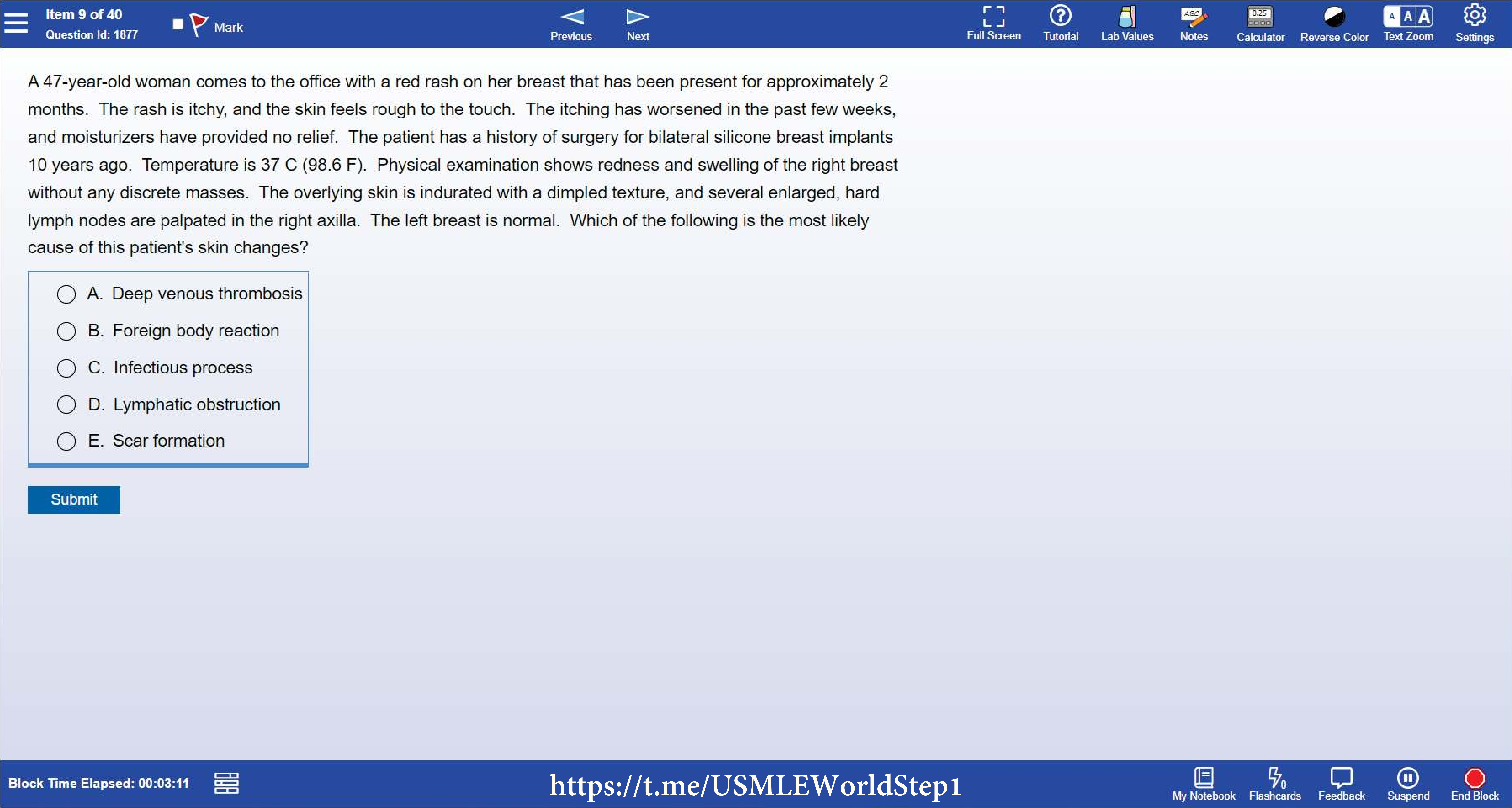
disease. The risk for permanent tubal scarring increases with inadequate antibiotic treatment due to persisting or prolonged infection of the upper genital tract.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A 47-year-old woman comes to the office with a red rash on her breast that has been present for approximately 2 months. The rash is itchy, and the skin feels rough to the touch. The itching has worsened in the past few weeks, and moisturizers have provided no relief. The patient has a history of surgery for bilateral silicone breast implants 10 years ago. Temperature is 37 C (98.6 F). Physical examination shows redness and swelling of the right breast without any discrete masses. The overlying skin is indurated with a dimpled texture, and several enlarged, hard lymph nodes are palpated in the right axilla. The left breast is normal. Which of the following is the most likely cause of this patient's skin changes?

○ A. Deep venous thrombosis
○ B. Foreign body reaction
○ C. Infectious process
○ D. Lymphatic obstruction
○ E. Scar formation

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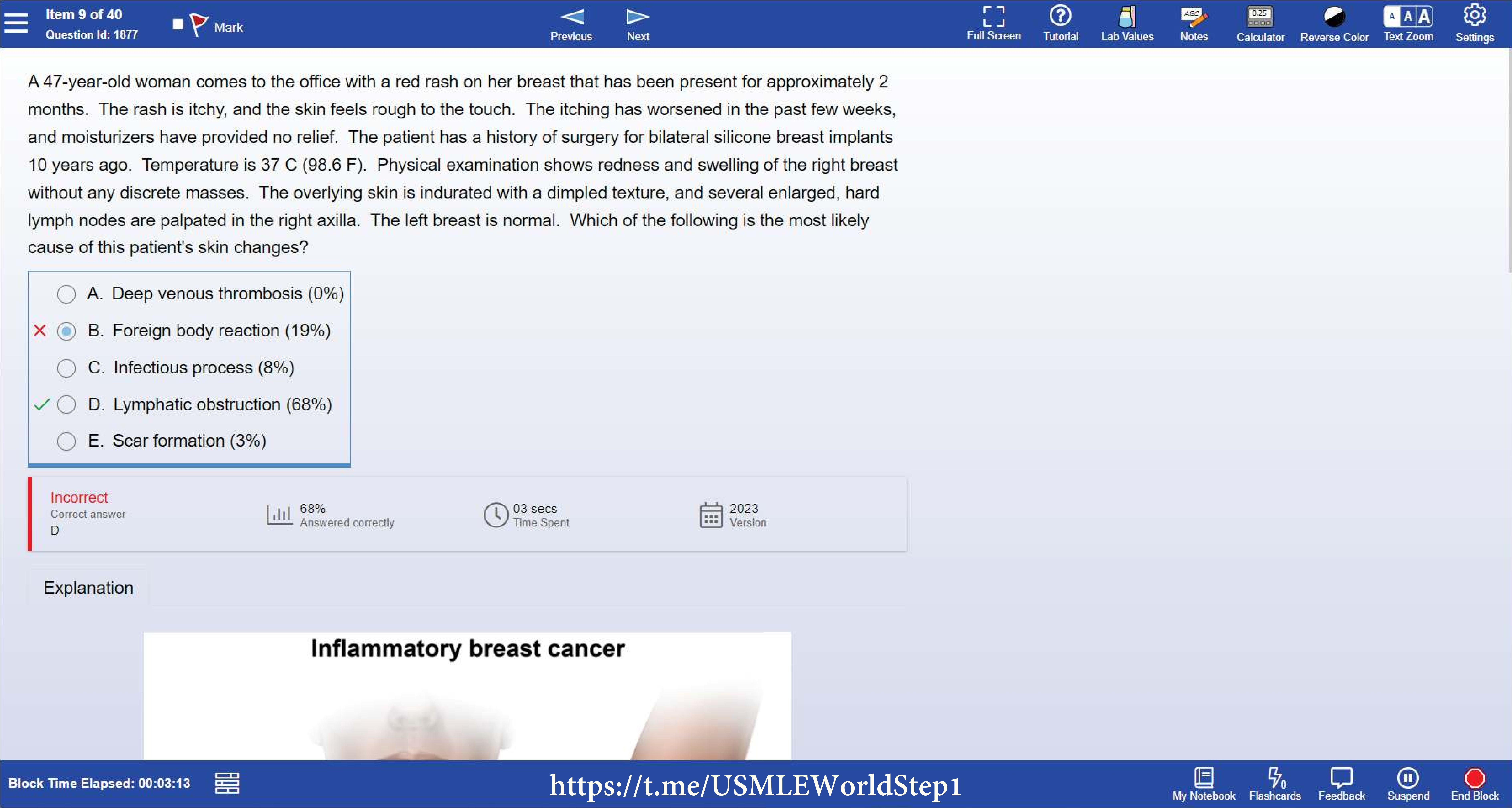
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- ○ A. Deep venous thrombosis (0%)
- ✗ ● B. Foreign body reaction (19%)
- ○ C. Infectious process (8%)
- ✓ ○ D. Lymphatic obstruction (68%)
- ○ E. Scar formation (3%)

Incorrect
Correct answer
D

68%
Answered correctly

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Explanation

Inflammatory breast cancer

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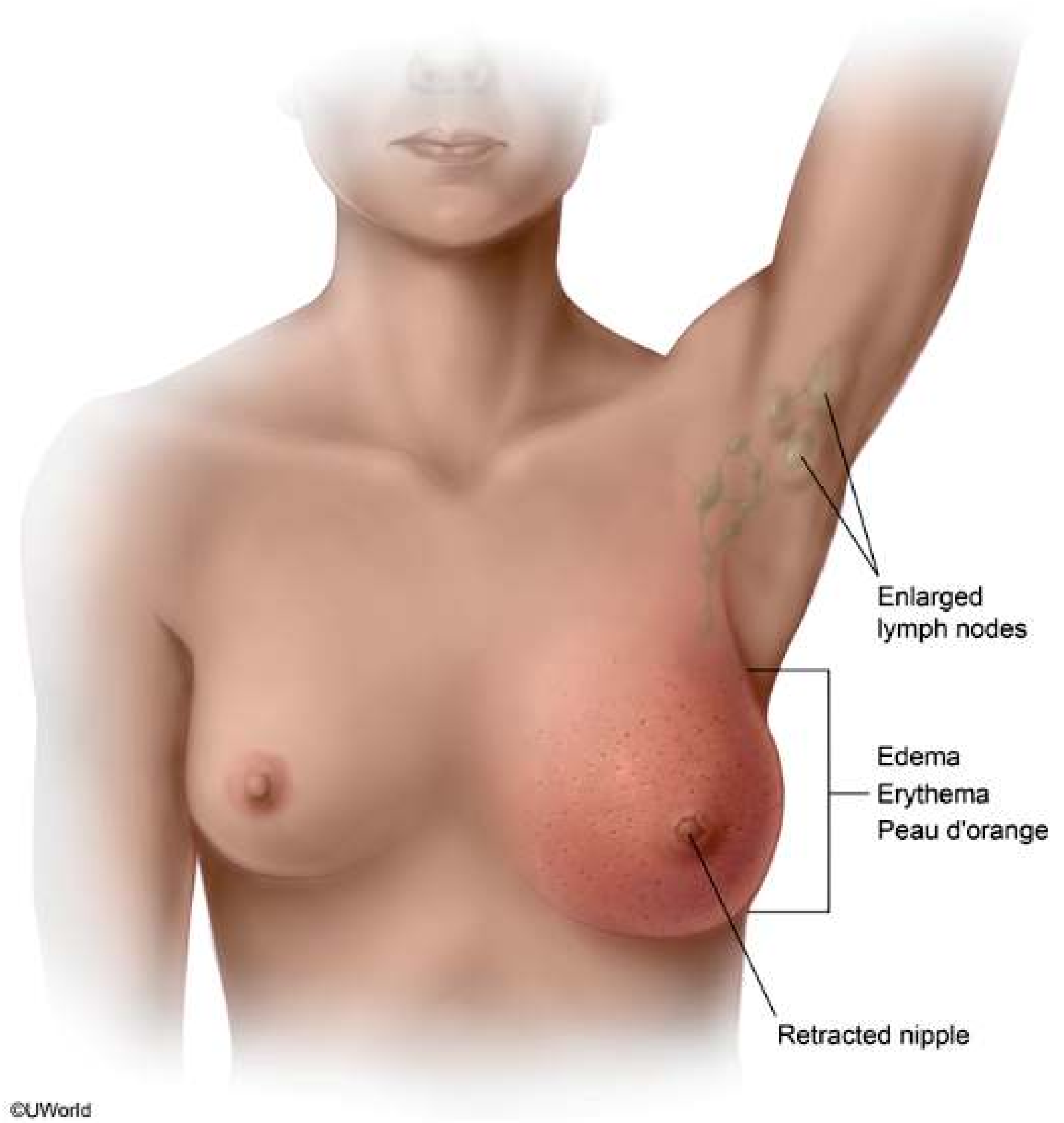
Inflammatory breast cancer


Enlarged
lymph nodes
Edema
Erythema
Peau d'orange
Retracted nipple
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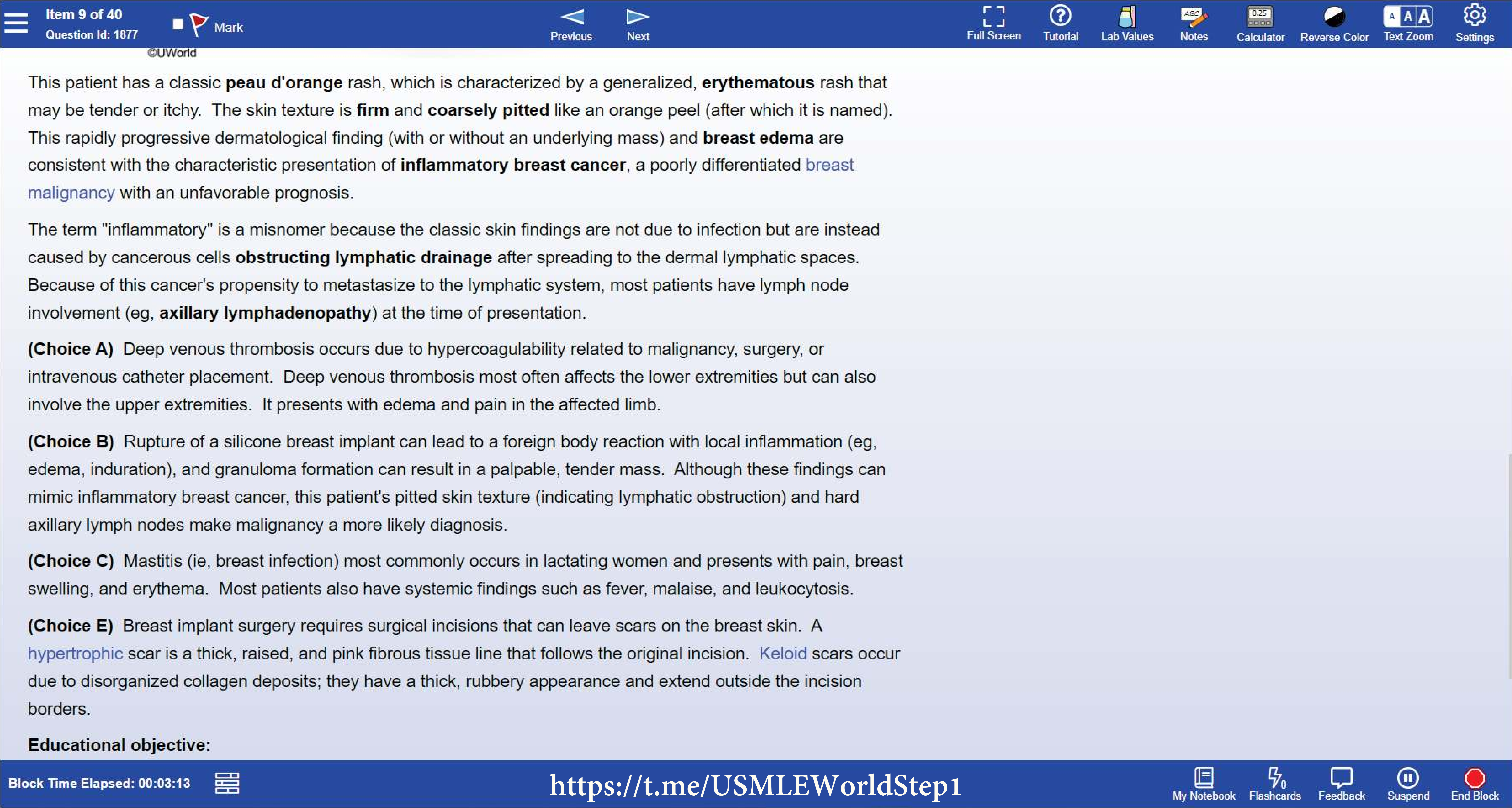

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This patient has a classic **peau d'orange** rash, which is characterized by a generalized, **erythematous** rash that may be tender or itchy. The skin texture is **firm** and **coarsely pitted** like an orange peel (after which it is named). This rapidly progressive dermatological finding (with or without an underlying mass) and **breast edema** are consistent with the characteristic presentation of **inflammatory breast cancer**, a poorly differentiated breast malignancy with an unfavorable prognosis.

The term "inflammatory" is a misnomer because the classic skin findings are not due to infection but are instead caused by cancerous cells **obstructing lymphatic drainage** after spreading to the dermal lymphatic spaces. Because of this cancer's propensity to metastasize to the lymphatic system, most patients have lymph node involvement (eg, **axillary lymphadenopathy**) at the time of presentation.

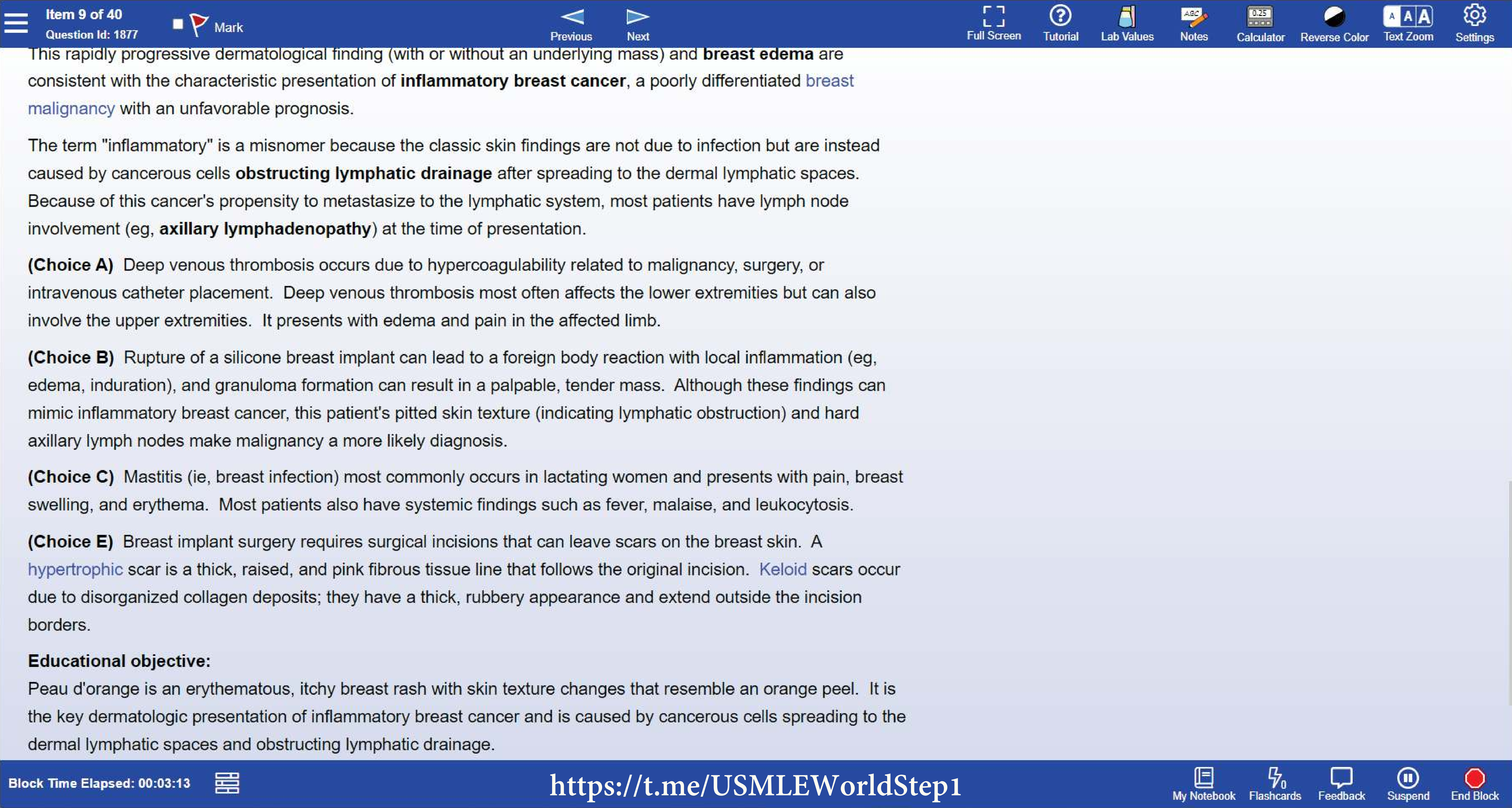
(Choice A) Deep venous thrombosis occurs due to hypercoagulability related to malignancy, surgery, or intravenous catheter placement. Deep venous thrombosis most often affects the lower extremities but can also involve the upper extremities. It presents with edema and pain in the affected limb.

(Choice B) Rupture of a silicone breast implant can lead to a foreign body reaction with local inflammation (eg, edema, induration), and granuloma formation can result in a palpable, tender mass. Although these findings can mimic inflammatory breast cancer, this patient's pitted skin texture (indicating lymphatic obstruction) and hard axillary lymph nodes make malignancy a more likely diagnosis.

(Choice C) Mastitis (ie, breast infection) most commonly occurs in lactating women and presents with pain, breast swelling, and erythema. Most patients also have systemic findings such as fever, malaise, and leukocytosis.

(Choice E) Breast implant surgery requires surgical incisions that can leave scars on the breast skin. A hypertrophic scar is a thick, raised, and pink fibrous tissue line that follows the original incision. Keloid scars occur due to disorganized collagen deposits; they have a thick, rubbery appearance and extend outside the incision borders.

Educational objective:



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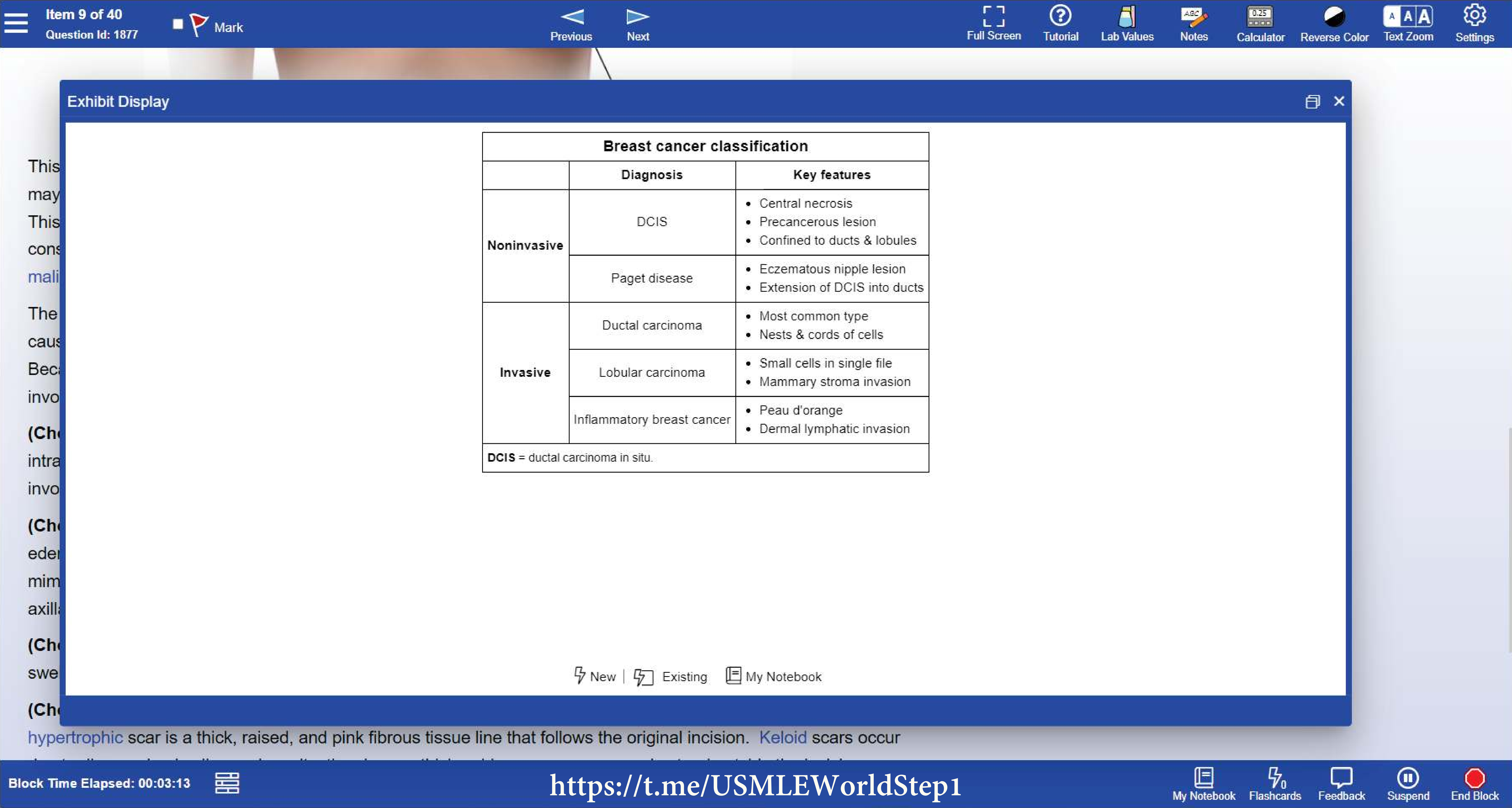
Educational objective:

Peau d'orange is an erythematous, itchy breast rash with skin texture changes that resemble an orange peel. It is the key dermatologic presentation of inflammatory breast cancer and is caused by cancerous cells spreading to the dermal lymphatic spaces and obstructing lymphatic drainage.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hypertrophic scar is a thick, raised, and pink fibrous tissue line that follows the original incision. Keloid scars occur

Breast cancer classification

	Diagnosis	Key features
Noninvasive	DCIS	- Central necrosis - Precancerous lesion - Confined to ducts & lobules
	Paget disease	- Eczematous nipple lesion - Extension of DCIS into ducts
Invasive	Ductal carcinoma	- Most common type - Nests & cords of cells
	Lobular carcinoma	- Small cells in single file - Mammary stroma invasion
	Inflammatory breast cancer	- Peau d'orange - Dermal lymphatic invasion

DCIS = ductal carcinoma in situ.

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The term "inflammatory" is a misnomer because the classic skin findings are not due to infection but are instead

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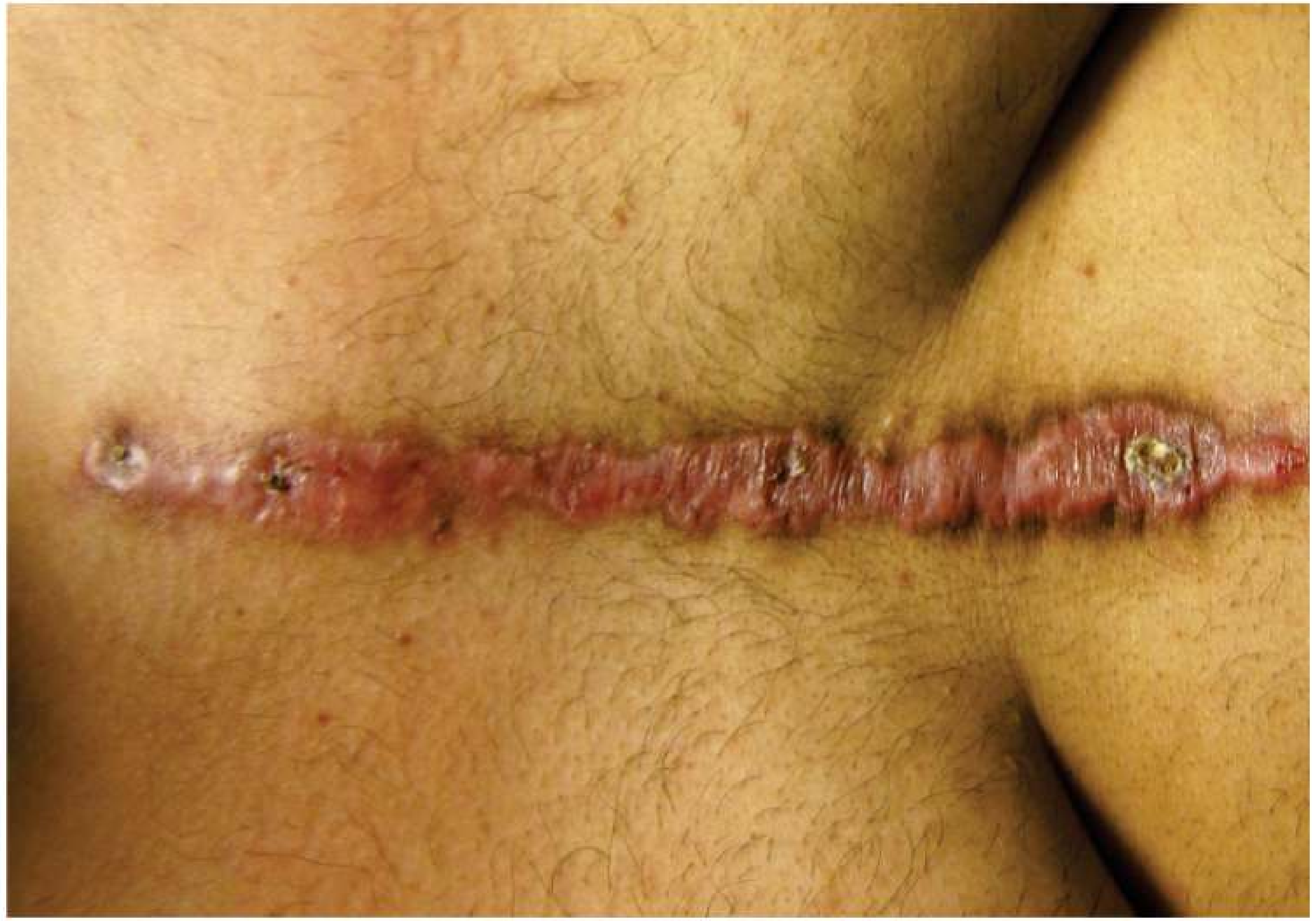

- Inflammatory breast cancer: an overview.

The term "inflammatory" is a misnomer because the classic skin findings are not due to infection but are instead

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- Inflammatory breast cancer: an overview.

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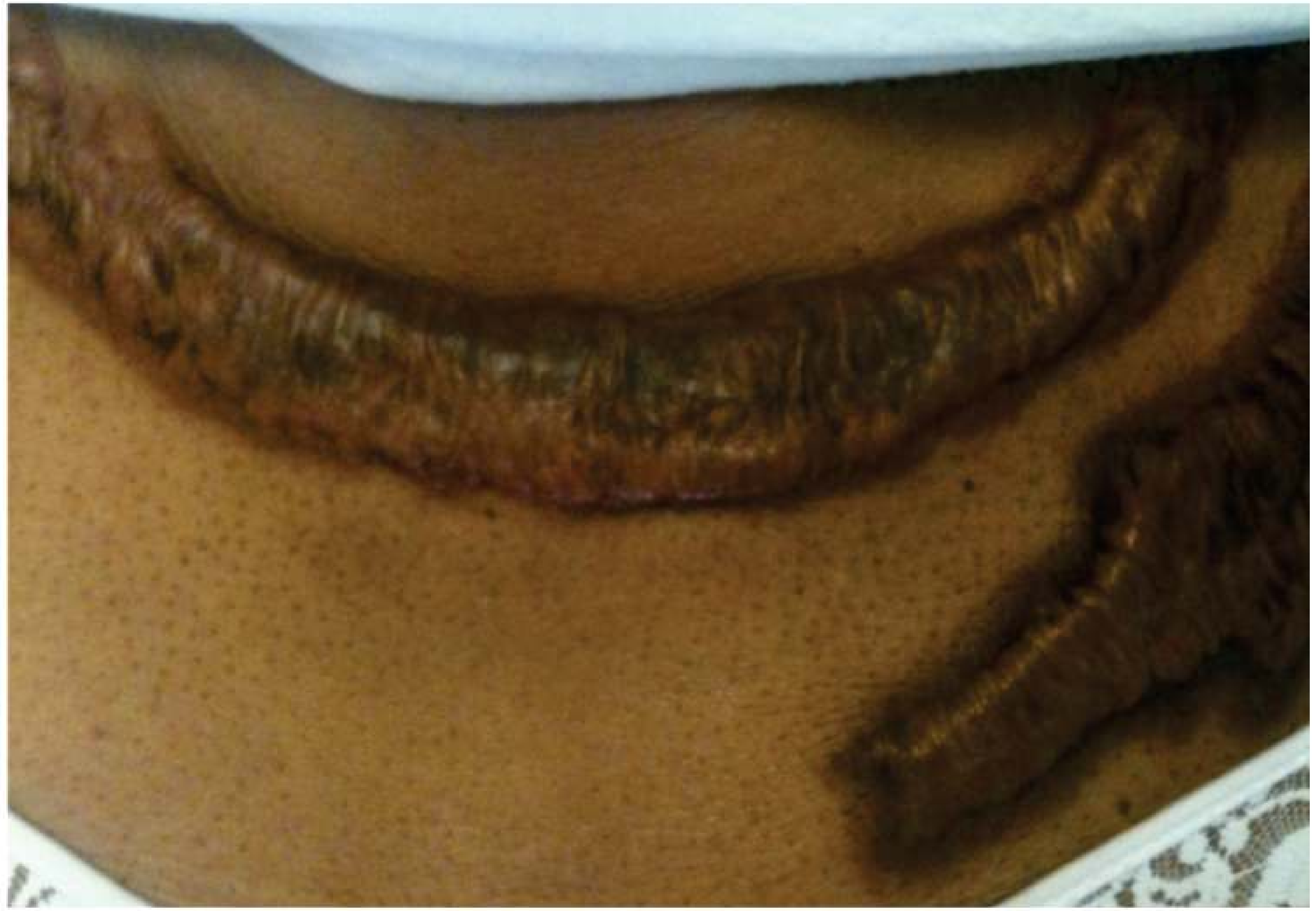

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A 49-year-old woman, gravida 2 para 2, comes to the office due to 10 months of irregular vaginal bleeding. The patient's last menstrual period was 3 years ago. She has a history of hypothyroidism and takes levothyroxine daily. Ultrasound reveals a thickened endometrium and a solid, left adnexal mass. Endometrial biopsy reveals hyperplasia, and the patient is scheduled for laparotomy. Intraoperatively, the ovarian mass is yellow and firm. Microscopic examination of the mass shows small, cuboidal cells in sheets as well as in a microfollicular pattern with gland-like structures containing eosinophilic material. Which of the following is most likely secreted by this patient's tumor?

○ A. α-Fetoprotein
○ B. β-hCG
○ C. Cancer antigen 125
○ D. Estrogen
○ E. Testosterone
○ F. Thyroxine

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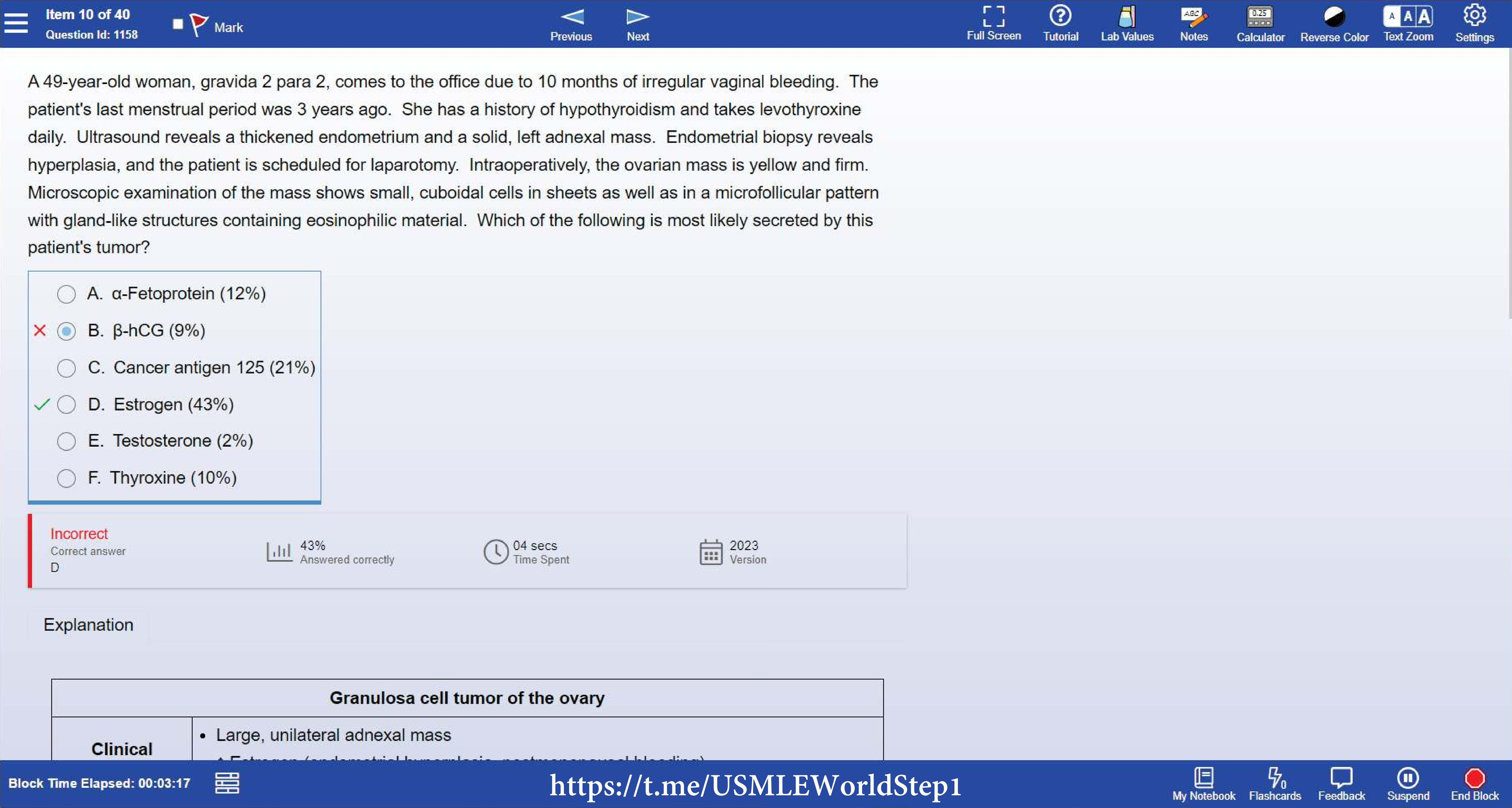
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○ A. α-Fetoprotein (12%)

✗ ● B. β-hCG (9%)

○ C. Cancer antigen 125 (21%)

✓ ○ D. Estrogen (43%)

○ E. Testosterone (2%)

○ F. Thyroxine (10%)

Incorrect
Correct answer
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43%
Answered correctly

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Explanation

Granulosa cell tumor of the ovary	
Clinical	• Large, unilateral adnexal mass

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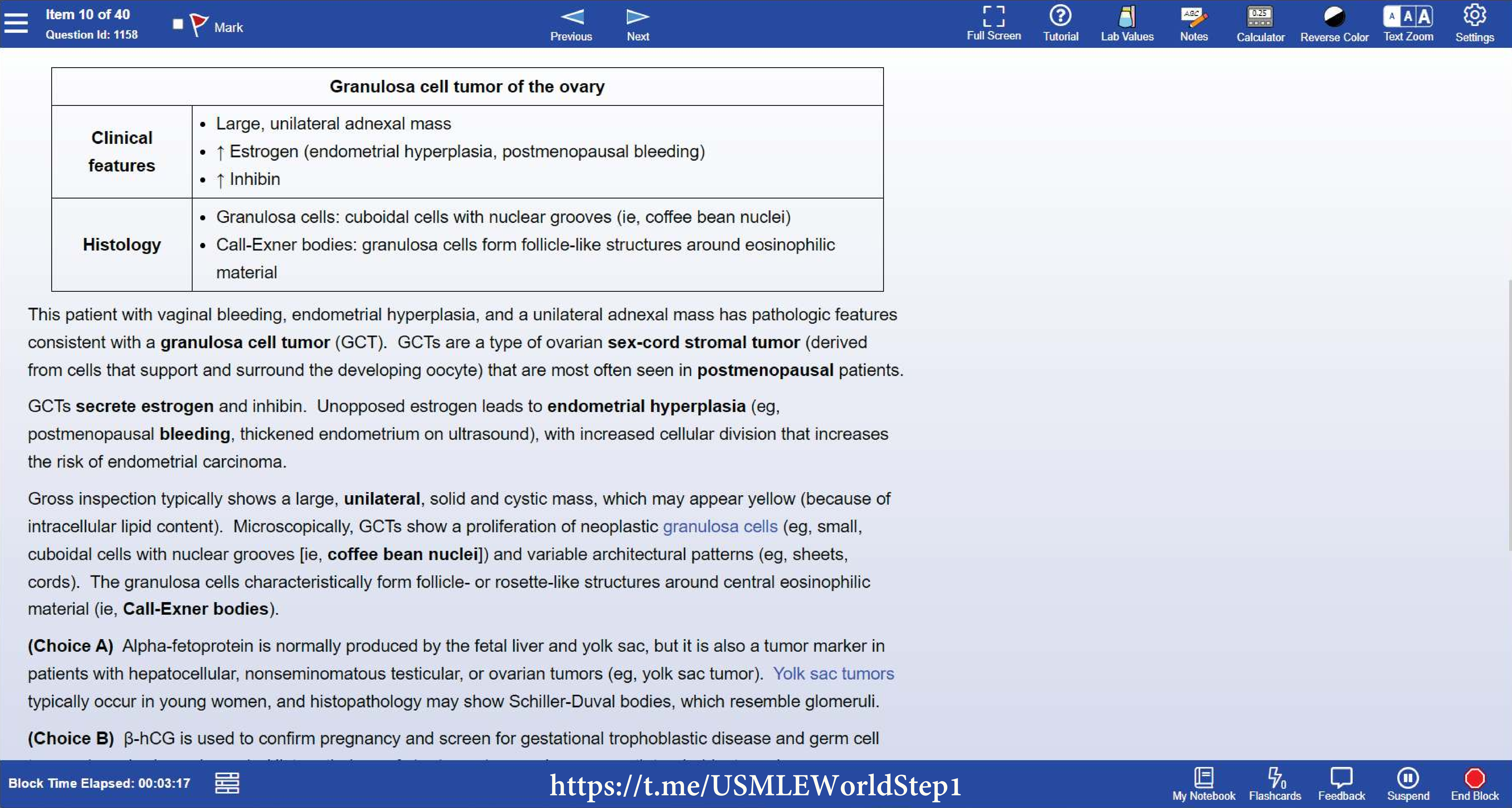
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Granulosa cell tumor of the ovary	
Clinical features	• Large, unilateral adnexal mass • ↑ Estrogen (endometrial hyperplasia, postmenopausal bleeding) • ↑ Inhibin
Histology	• Granulosa cells: cuboidal cells with nuclear grooves (ie, coffee bean nuclei) • Call-Exner bodies: granulosa cells form follicle-like structures around eosinophilic material

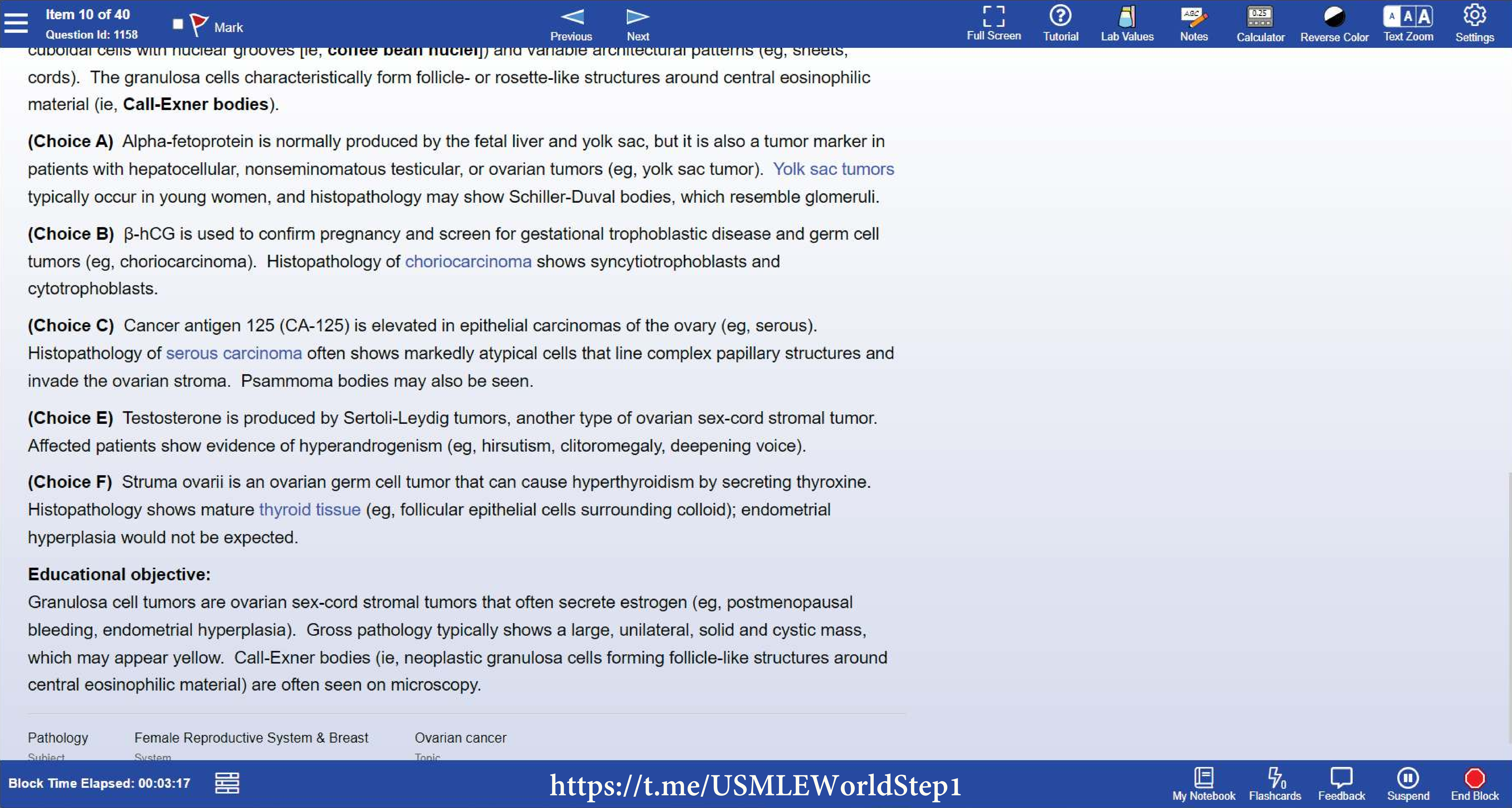
This patient with vaginal bleeding, endometrial hyperplasia, and a unilateral adnexal mass has pathologic features consistent with a **granulosa cell tumor** (GCT). GCTs are a type of ovarian **sex-cord stromal tumor** (derived from cells that support and surround the developing oocyte) that are most often seen in **postmenopausal** patients.

GCTs **secrete estrogen** and inhibin. Unopposed estrogen leads to **endometrial hyperplasia** (eg, postmenopausal **bleeding**, thickened endometrium on ultrasound), with increased cellular division that increases the risk of endometrial carcinoma.

Gross inspection typically shows a large, **unilateral**, solid and cystic mass, which may appear yellow (because of intracellular lipid content). Microscopically, GCTs show a proliferation of neoplastic granulosa cells (eg, small, cuboidal cells with nuclear grooves [ie, **coffee bean nuclei**]) and variable architectural patterns (eg, sheets, cords). The granulosa cells characteristically form follicle- or rosette-like structures around central eosinophilic material (ie, **Call-Exner bodies**).

(Choice A) Alpha-fetoprotein is normally produced by the fetal liver and yolk sac, but it is also a tumor marker in patients with hepatocellular, nonseminomatous testicular, or ovarian tumors (eg, yolk sac tumor). Yolk sac tumors typically occur in young women, and histopathology may show Schiller-Duval bodies, which resemble glomeruli.

(Choice B) β-hCG is used to confirm pregnancy and screen for gestational trophoblastic disease and germ cell



cuboidal cells with nuclear grooves [ie, **coffee bean nuclei**]) and variable architectural patterns (eg, sheets, cords). The granulosa cells characteristically form follicle- or rosette-like structures around central eosinophilic material (ie, **Call-Exner bodies**).

(Choice A) Alpha-fetoprotein is normally produced by the fetal liver and yolk sac, but it is also a tumor marker in patients with hepatocellular, nonseminomatous testicular, or ovarian tumors (eg, yolk sac tumor). Yolk sac tumors typically occur in young women, and histopathology may show Schiller-Duval bodies, which resemble glomeruli.

(Choice B) β-hCG is used to confirm pregnancy and screen for gestational trophoblastic disease and germ cell tumors (eg, choriocarcinoma). Histopathology of choriocarcinoma shows syncytiotrophoblasts and cytotrophoblasts.

(Choice C) Cancer antigen 125 (CA-125) is elevated in epithelial carcinomas of the ovary (eg, serous). Histopathology of serous carcinoma often shows markedly atypical cells that line complex papillary structures and invade the ovarian stroma. Psammoma bodies may also be seen.

(Choice E) Testosterone is produced by Sertoli-Leydig tumors, another type of ovarian sex-cord stromal tumor. Affected patients show evidence of hyperandrogenism (eg, hirsutism, clitoromegaly, deepening voice).

(Choice F) Struma ovarii is an ovarian germ cell tumor that can cause hyperthyroidism by secreting thyroxine. Histopathology shows mature thyroid tissue (eg, follicular epithelial cells surrounding colloid); endometrial hyperplasia would not be expected.

Educational objective:

Granulosa cell tumors are ovarian sex-cord stromal tumors that often secrete estrogen (eg, postmenopausal bleeding, endometrial hyperplasia). Gross pathology typically shows a large, unilateral, solid and cystic mass, which may appear yellow. Call-Exner bodies (ie, neoplastic granulosa cells forming follicle-like structures around central eosinophilic material) are often seen on microscopy.

Pathology Subject	Female Reproductive System & Breast System	Ovarian cancer Topic

- Granulosa cells: cuboidal cells with nuclear grooves (ie, coffee bean nuclei)

Histology

- Call-Exner bodies: granulosa cells form follicle-like structures around eosinophilic

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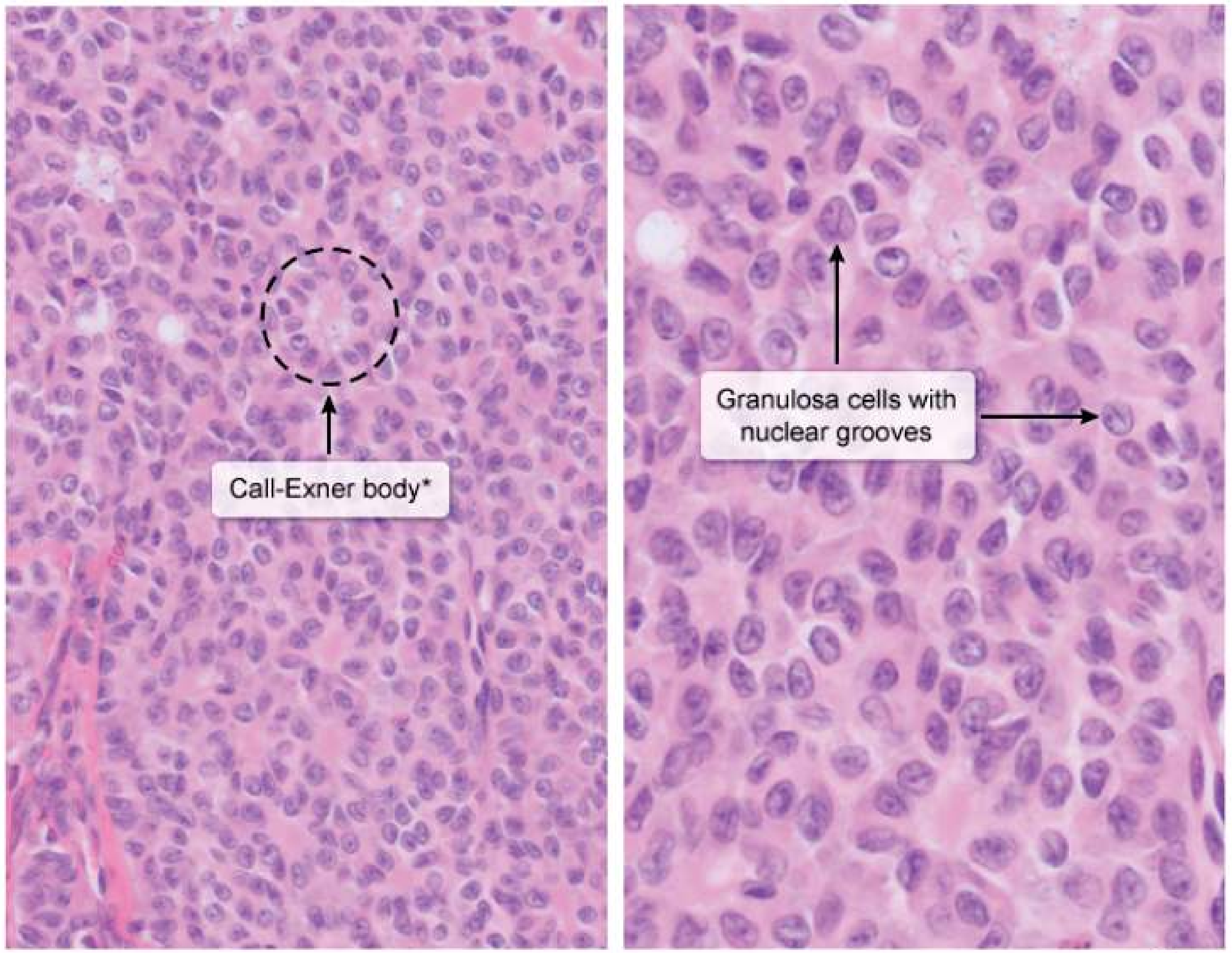
Granulosa cell tumor



*Granulosa cells lining eosinophilic material

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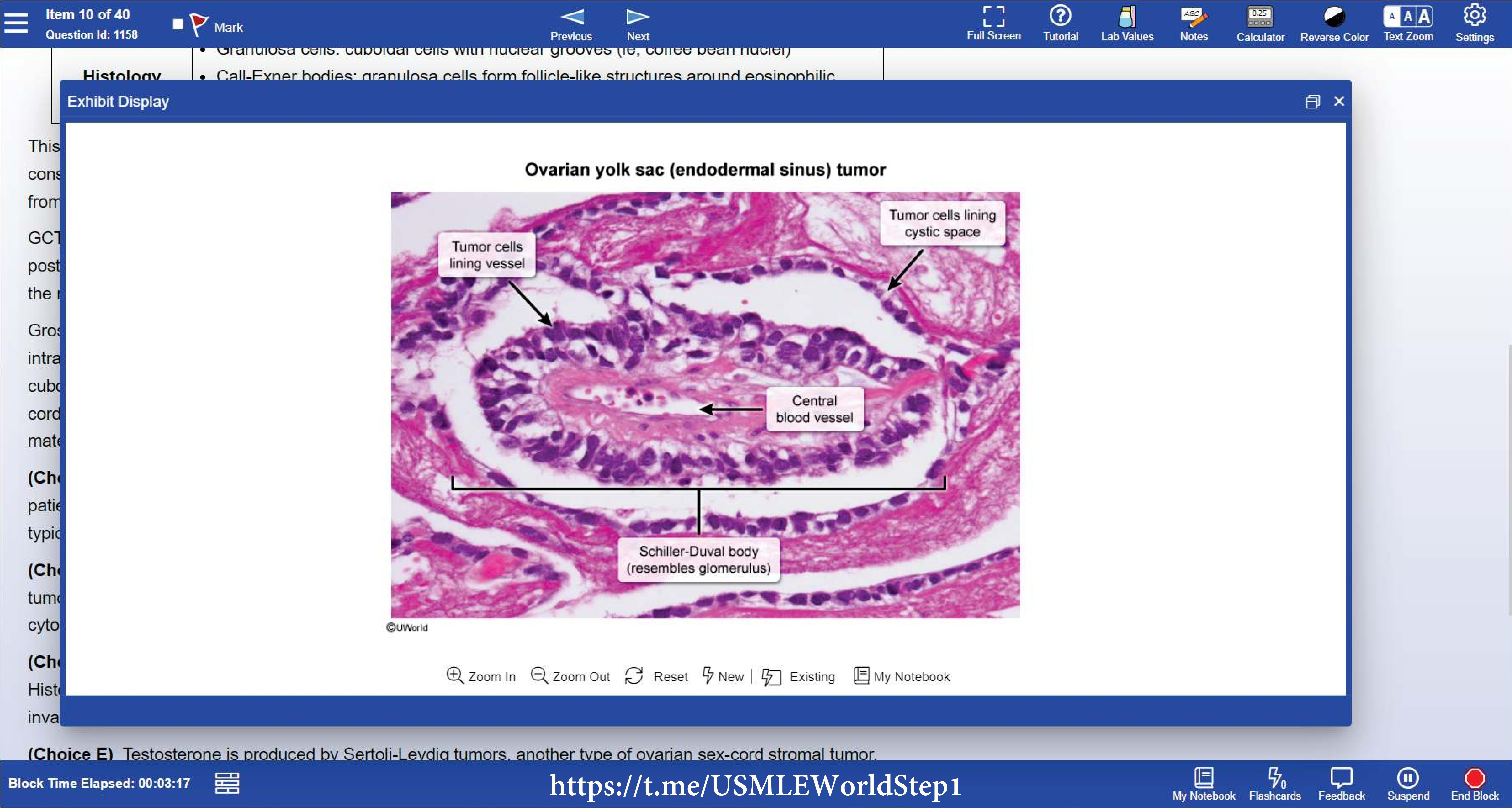
(Choice E) Testosterone is produced by Sertoli-Leydig tumors, another type of ovarian sex-cord stromal tumor.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- Granulosa cells: cuboidal cells with nuclear grooves (ie, coffee bean nuclei)

Histology

- Call-Exner bodies: granulosa cells form follicle-like structures around eosinophilic

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Ovarian yolk sac (endodermal sinus) tumor

Tumor cells lining cystic space
Tumor cells lining vessel
Central blood vessel
Schiller-Duval body (resembles glomerulus)

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(Choice E) Testosterone is produced by Sertoli-Leydig tumors, another type of ovarian sex-cord stromal tumor.

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- Granulosa cells: cuboidal cells with nuclear grooves (ie, coffee bean nuclei)

Histology

- Call-Exner bodies: granulosa cells form follicle-like structures around eosinophilic

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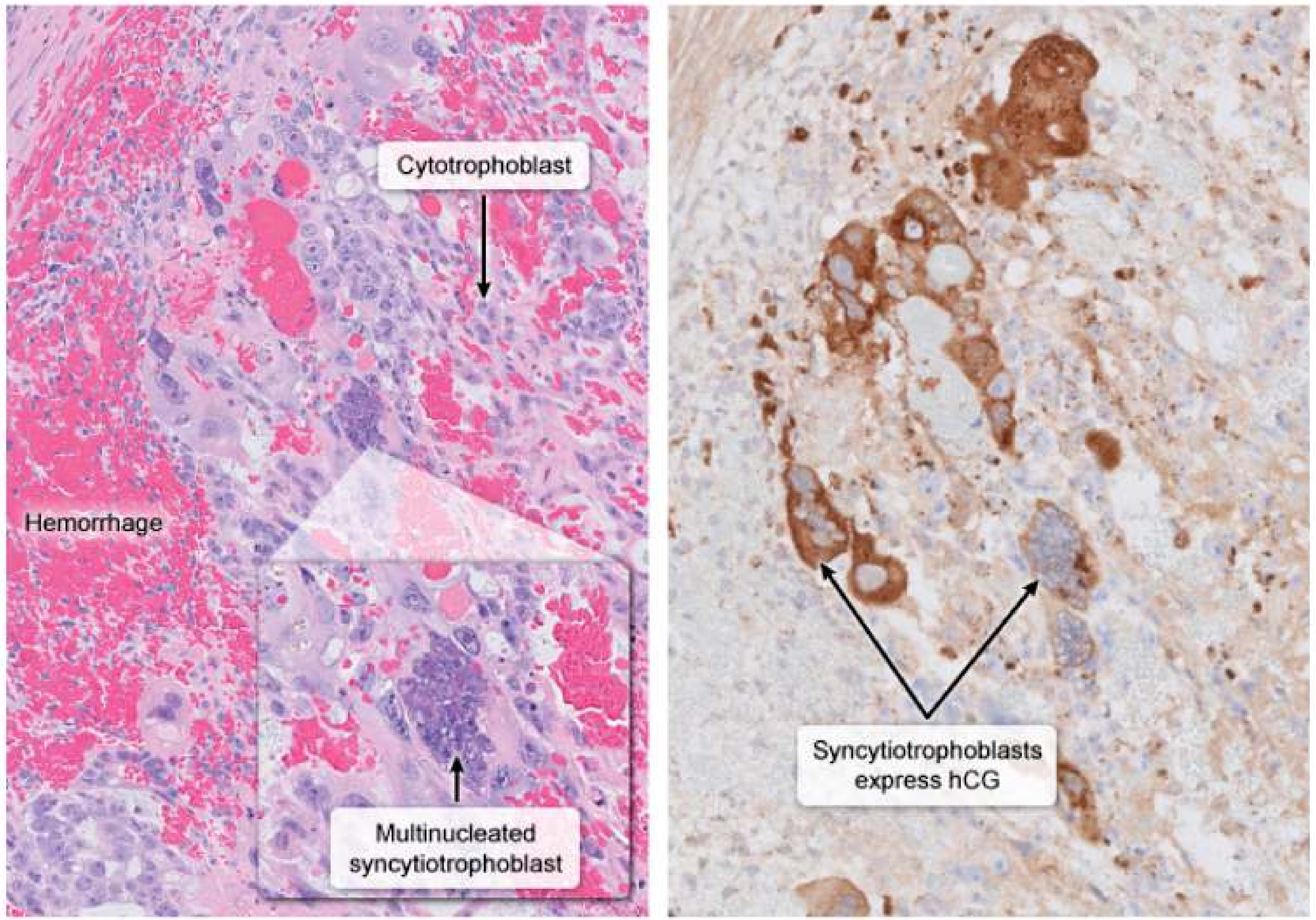
Choriocarcinoma


Cytotrophoblast
Hemorrhage
Multinucleated syncytiotrophoblast
Syncytiotrophoblasts express hCG

Hematoxylin & eosin stain

Human chorionic gonadotropin (hCG) stain

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(Choice E) Testosterone is produced by Sertoli-Leydig tumors, another type of ovarian sex-cord stromal tumor.

Histology	- Granulosa cells: cuboidal cells with nuclear grooves (ie, coffee bean nuclei) - Call-Exner bodies: granulosa cells form follicle-like structures around eosinophilic

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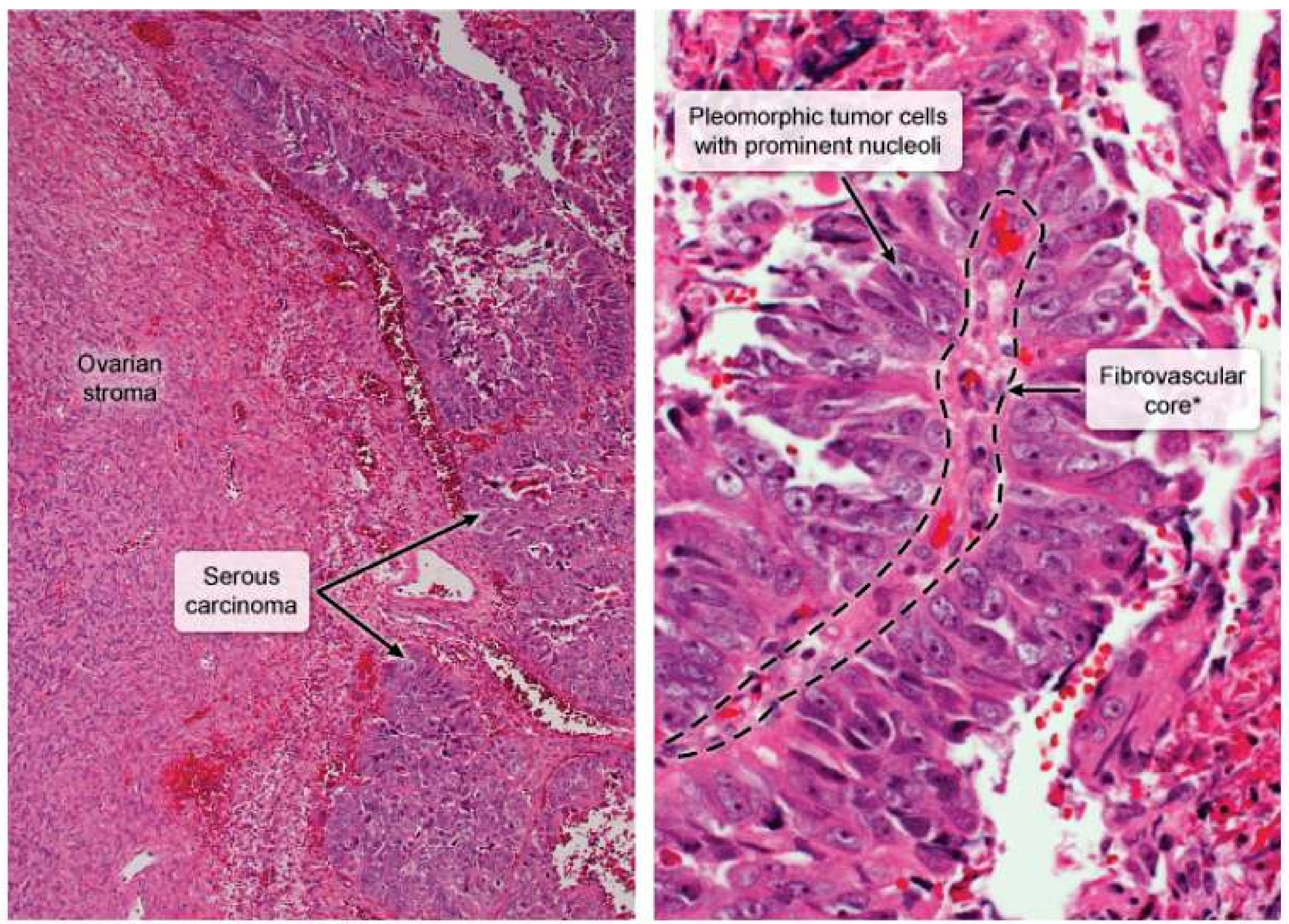
High-grade serous ovarian carcinoma


Ovarian stroma
Serous carcinoma
Pleomorphic tumor cells with prominent nuclei
Fibrovascular core*

*Papillary architecture: tumor cells lining fibrovascular core.

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(Choice E) Testosterone is produced by Sertoli-Leydig tumors, another type of ovarian sex-cord stromal tumor.

Gross inspection typically shows a large **unilateral**, solid and cystic mass, which may appear yellow (because of

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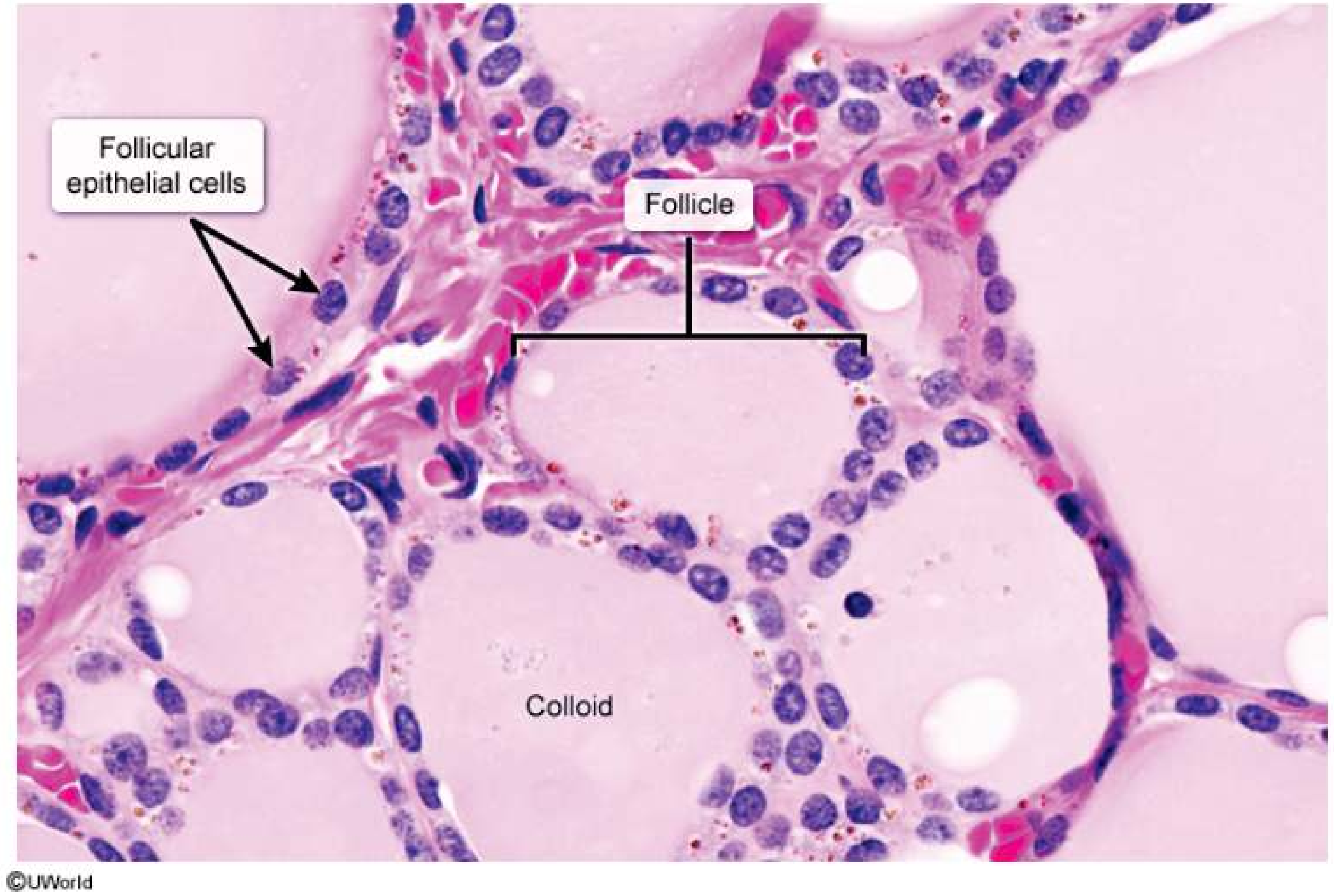
Normal thyroid gland



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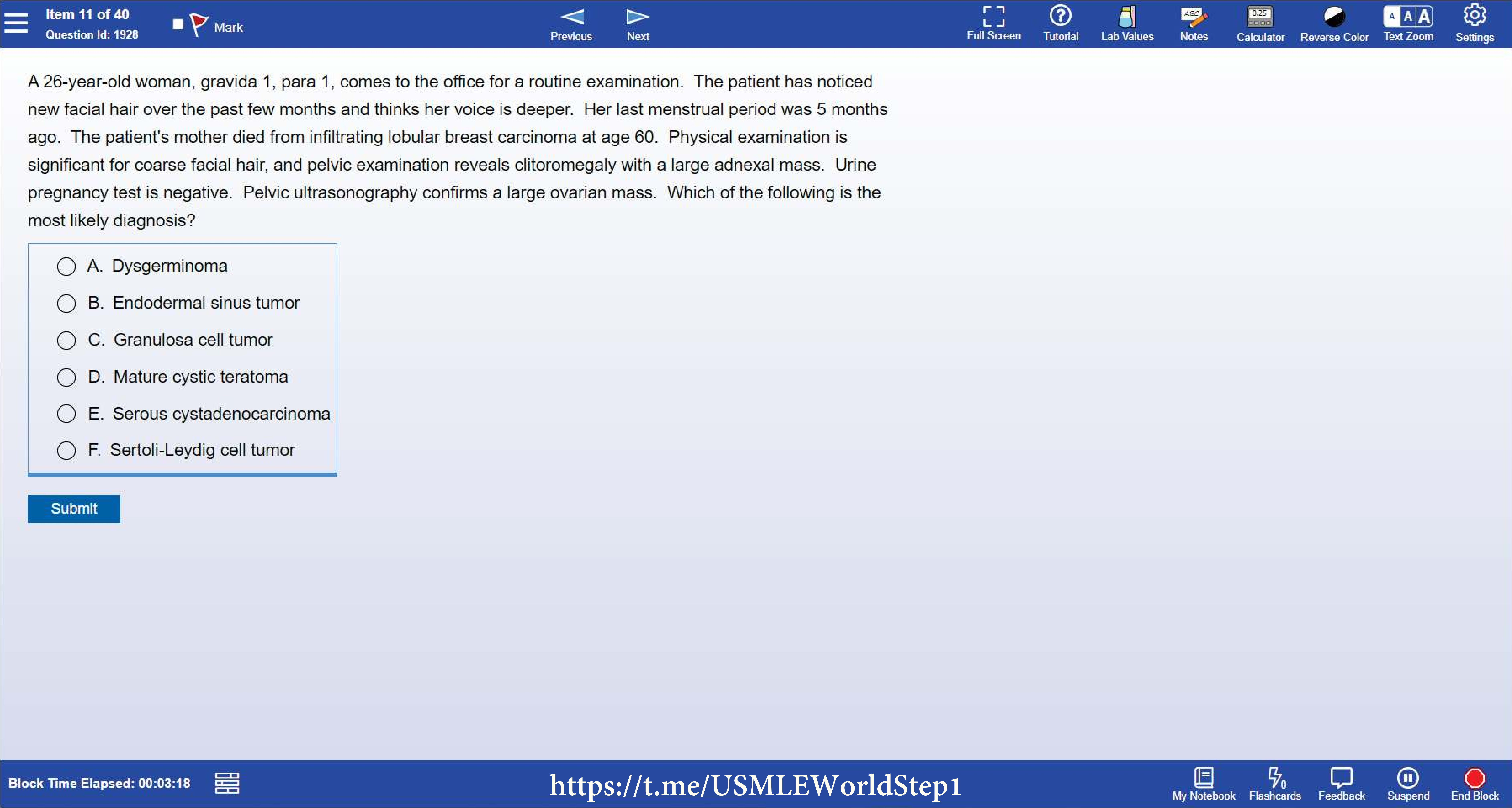
which may appear yellow. Call-Exner bodies (ie, neoplastic granulosa cells forming follicle-like structures around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A 26-year-old woman, gravida 1, para 1, comes to the office for a routine examination. The patient has noticed new facial hair over the past few months and thinks her voice is deeper. Her last menstrual period was 5 months ago. The patient's mother died from infiltrating lobular breast carcinoma at age 60. Physical examination is significant for coarse facial hair, and pelvic examination reveals clitoromegaly with a large adnexal mass. Urine pregnancy test is negative. Pelvic ultrasonography confirms a large ovarian mass. Which of the following is the most likely diagnosis?

- ○ A. Dysgerminoma
- ○ B. Endodermal sinus tumor
- ○ C. Granulosa cell tumor
- ○ D. Mature cystic teratoma
- ○ E. Serous cystadenocarcinoma
- ○ F. Sertoli-Leydig cell tumor

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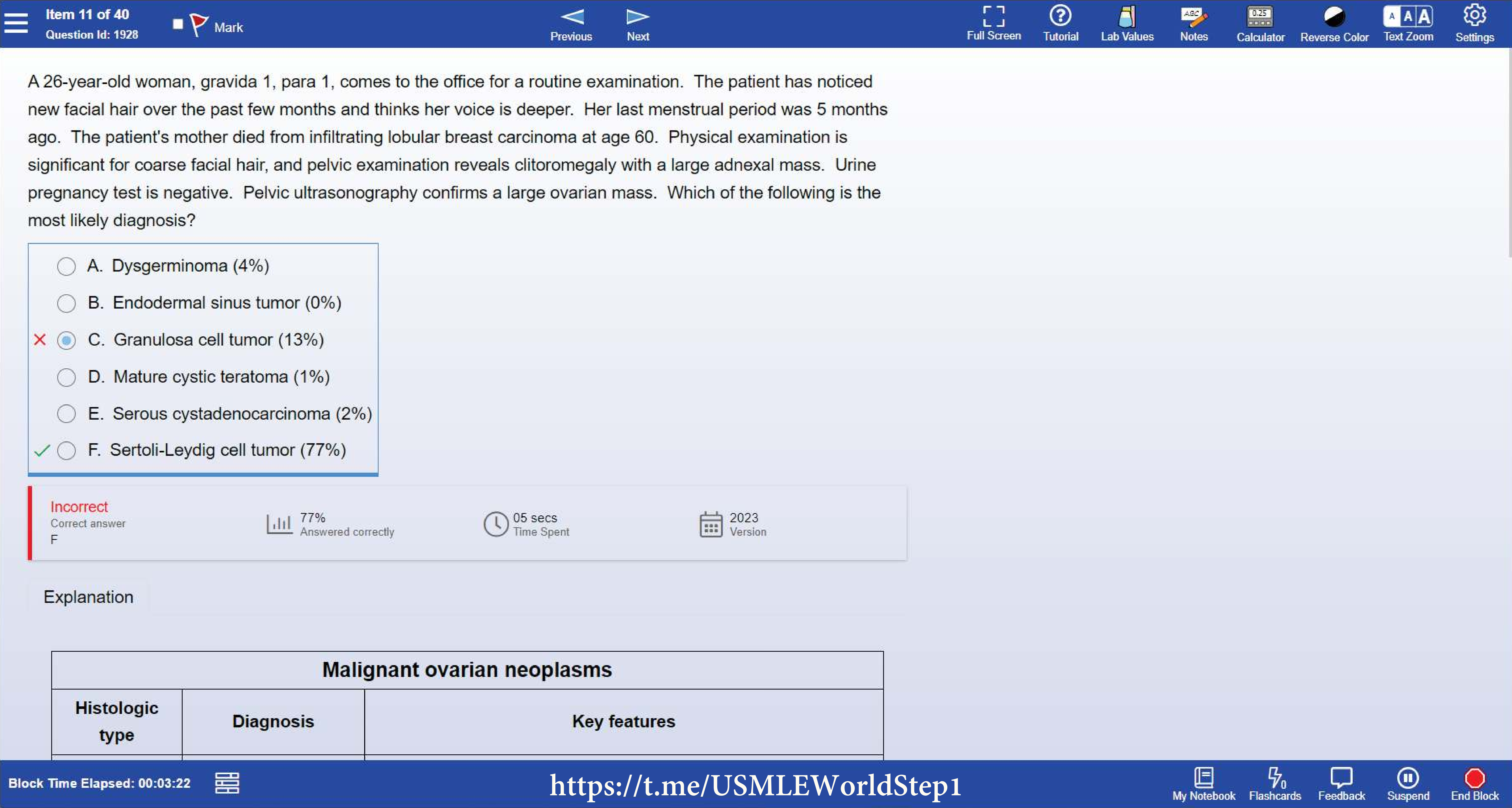
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A 26-year-old woman, gravida 1, para 1, comes to the office for a routine examination. The patient has noticed new facial hair over the past few months and thinks her voice is deeper. Her last menstrual period was 5 months ago. The patient's mother died from infiltrating lobular breast carcinoma at age 60. Physical examination is significant for coarse facial hair, and pelvic examination reveals clitoromegaly with a large adnexal mass. Urine pregnancy test is negative. Pelvic ultrasonography confirms a large ovarian mass. Which of the following is the most likely diagnosis?

- ○ A. Dysgerminoma (4%)
- ○ B. Endodermal sinus tumor (0%)
- ✗ ● C. Granulosa cell tumor (13%)
- ○ D. Mature cystic teratoma (1%)
- ○ E. Serous cystadenocarcinoma (2%)
- ✓ ○ F. Sertoli-Leydig cell tumor (77%)

Incorrect
Correct answer
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77%
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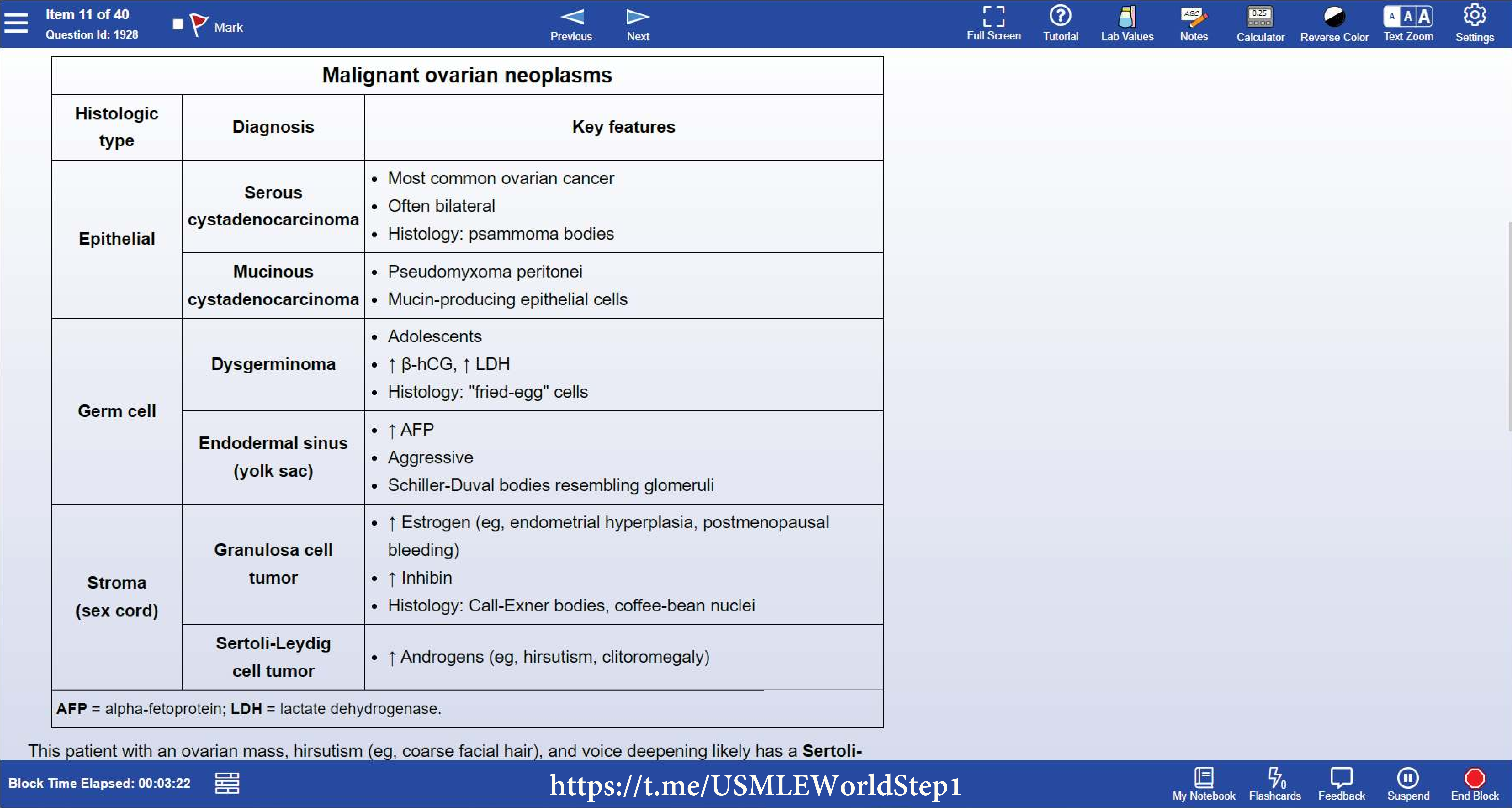
Explanation

Malignant ovarian neoplasms		
Histologic type	Diagnosis	Key features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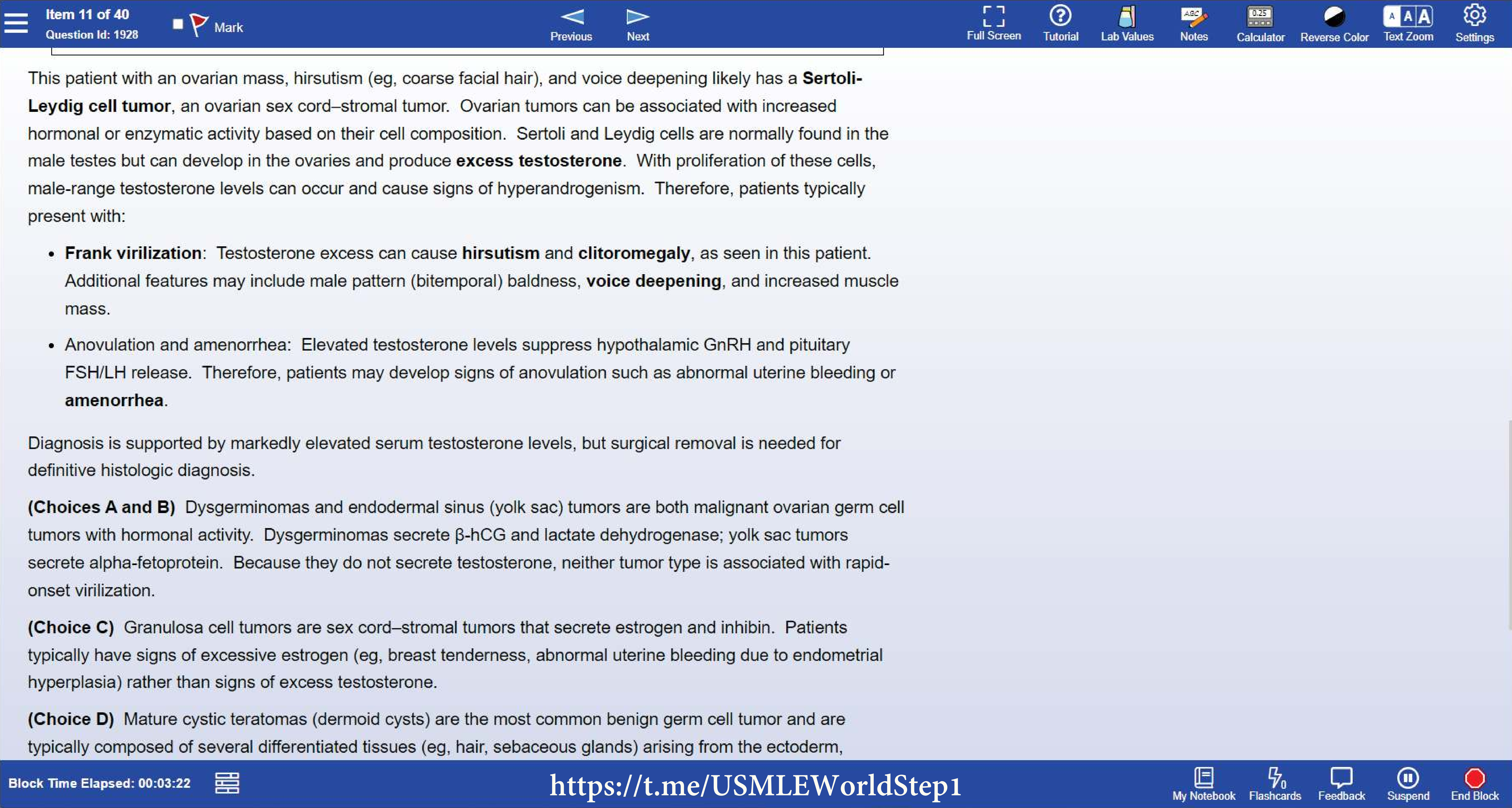
Malignant ovarian neoplasms

Histologic type	Diagnosis	Key features
Epithelial	**Serous cystadenocarcinoma**	• Most common ovarian cancer • Often bilateral • Histology: psammoma bodies
	Mucinous cystadenocarcinoma	• Pseudomyxoma peritonei • Mucin-producing epithelial cells
Germ cell	**Dysgerminoma**	• Adolescents • ↑ β-hCG, ↑ LDH • Histology: "fried-egg" cells
	Endodermal sinus (yolk sac)	• ↑ AFP • Aggressive • Schiller-Duval bodies resembling glomeruli
Stroma (sex cord)	**Granulosa cell tumor**	• ↑ Estrogen (eg, endometrial hyperplasia, postmenopausal bleeding) • ↑ Inhibin • Histology: Call-Exner bodies, coffee-bean nuclei
	Sertoli-Leydig cell tumor	• ↑ Androgens (eg, hirsutism, clitoromegaly)

AFP = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

This patient with an ovarian mass, hirsutism (eg, coarse facial hair), and voice deepening likely has a **Sertoli-**



This patient with an ovarian mass, hirsutism (eg, coarse facial hair), and voice deepening likely has a **Sertoli-Leydig cell tumor**, an ovarian sex cord–stromal tumor. Ovarian tumors can be associated with increased hormonal or enzymatic activity based on their cell composition. Sertoli and Leydig cells are normally found in the male testes but can develop in the ovaries and produce **excess testosterone**. With proliferation of these cells, male-range testosterone levels can occur and cause signs of hyperandrogenism. Therefore, patients typically present with:

- **Frank virilization**: Testosterone excess can cause **hirsutism** and **clitoromegaly**, as seen in this patient. Additional features may include male pattern (bitemporal) baldness, **voice deepening**, and increased muscle mass.
- Anovulation and amenorrhea: Elevated testosterone levels suppress hypothalamic GnRH and pituitary FSH/LH release. Therefore, patients may develop signs of anovulation such as abnormal uterine bleeding or **amenorrhea**.

Diagnosis is supported by markedly elevated serum testosterone levels, but surgical removal is needed for definitive histologic diagnosis.

(Choices A and B) Dysgerminomas and endodermal sinus (yolk sac) tumors are both malignant ovarian germ cell tumors with hormonal activity. Dysgerminomas secrete β-hCG and lactate dehydrogenase; yolk sac tumors secrete alpha-fetoprotein. Because they do not secrete testosterone, neither tumor type is associated with rapid-onset virilization.

(Choice C) Granulosa cell tumors are sex cord–stromal tumors that secrete estrogen and inhibin. Patients typically have signs of excessive estrogen (eg, breast tenderness, abnormal uterine bleeding due to endometrial hyperplasia) rather than signs of excess testosterone.

(Choice D) Mature cystic teratomas (dermoid cysts) are the most common benign germ cell tumor and are typically composed of several differentiated tissues (eg, hair, sebaceous glands) arising from the ectoderm,

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amenorrhea.

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(Choice C) Granulosa cell tumors are sex cord–stromal tumors that secrete estrogen and inhibin. Patients typically have signs of excessive estrogen (eg, breast tenderness, abnormal uterine bleeding due to endometrial hyperplasia) rather than signs of excess testosterone.

(Choice D) Mature cystic teratomas (dermoid cysts) are the most common benign germ cell tumor and are typically composed of several differentiated tissues (eg, hair, sebaceous glands) arising from the ectoderm, mesoderm, and endoderm. Most mature cystic teratomas do not produce hormones. The exception is struma ovarii, a monodermal teratoma mostly composed of thyroid tissue that can secrete thyroid hormone and cause signs of hyperthyroidism (eg, tachycardia, weight loss).

(Choice E) Serous cystadenocarcinomas are the most common epithelial ovarian cancer but typically have no hormonal or enzymatic activity.

Educational objective:

Sertoli-Leydig cell tumors of the ovary arise from the sex cord stroma and secrete testosterone. Therefore, patients typically have signs and symptoms of hyperandrogenism, including rapid-onset virilization (eg, hirsutism, clitoromegaly, voice deepening) and amenorrhea.

References

- Sertoli-leydig cell tumor of ovary—a diagnostic dilemma.

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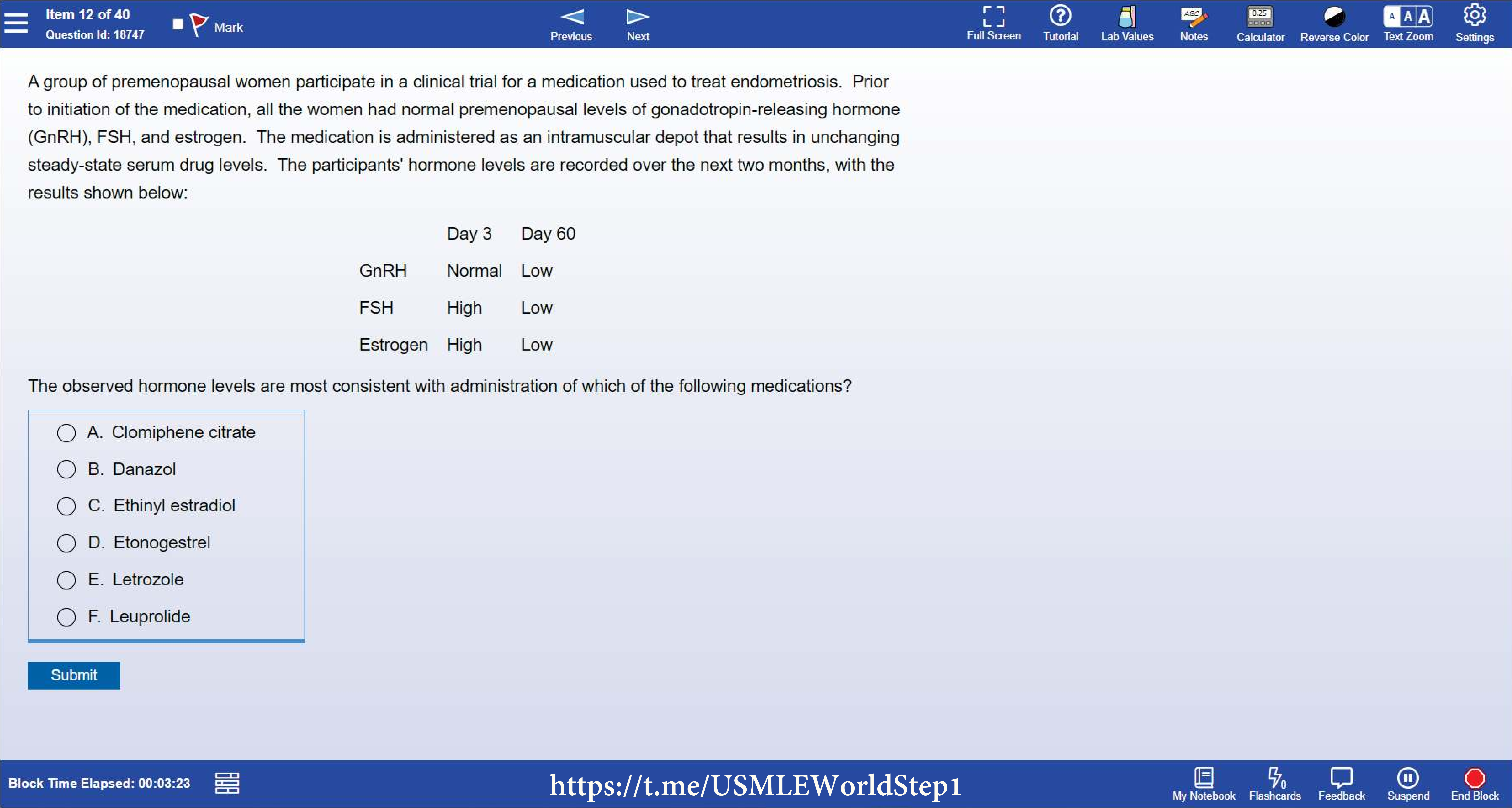
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A group of premenopausal women participate in a clinical trial for a medication used to treat endometriosis. Prior to initiation of the medication, all the women had normal premenopausal levels of gonadotropin-releasing hormone (GnRH), FSH, and estrogen. The medication is administered as an intramuscular depot that results in unchanging steady-state serum drug levels. The participants' hormone levels are recorded over the next two months, with the results shown below:

	Day 3	Day 60
GnRH	Normal	Low
FSH	High	Low
Estrogen	High	Low

The observed hormone levels are most consistent with administration of which of the following medications?

- ○ A. Clomiphene citrate
- ○ B. Danazol
- ○ C. Ethinyl estradiol
- ○ D. Etonogestrel
- ○ E. Letrozole
- ○ F. Leuprolide

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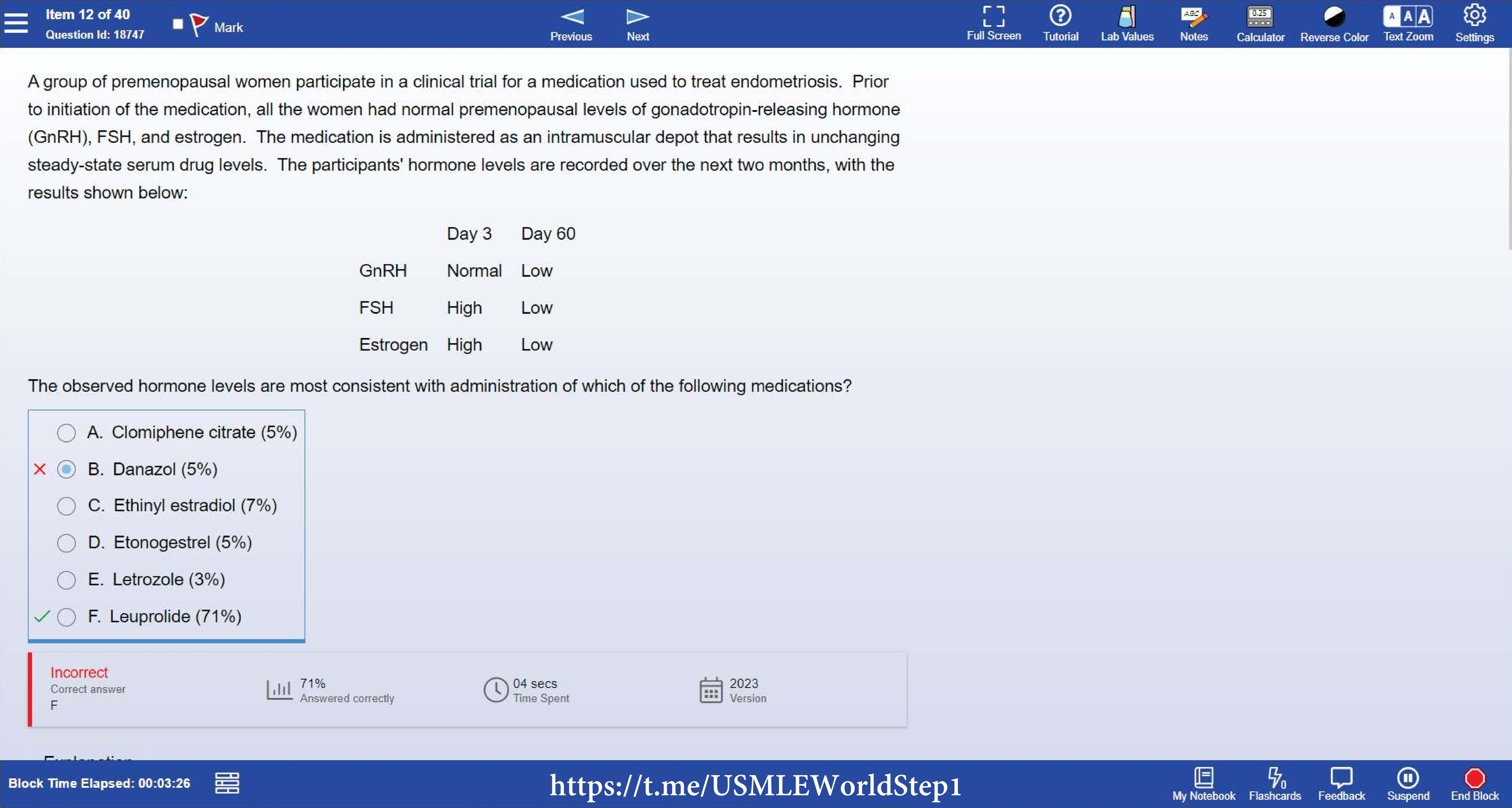
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	Day 3	Day 60
GnRH	Normal	Low
FSH	High	Low
Estrogen	High	Low

The observed hormone levels are most consistent with administration of which of the following medications?

- ○ A. Clomiphene citrate (5%)
- ✗ ● B. Danazol (5%)
- ○ C. Ethinyl estradiol (7%)
- ○ D. Etonogestrel (5%)
- ○ E. Letrozole (3%)
- ✓ ○ F. Leuprolide (71%)

Incorrect
Correct answer
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71%
Answered correctly

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Explanation

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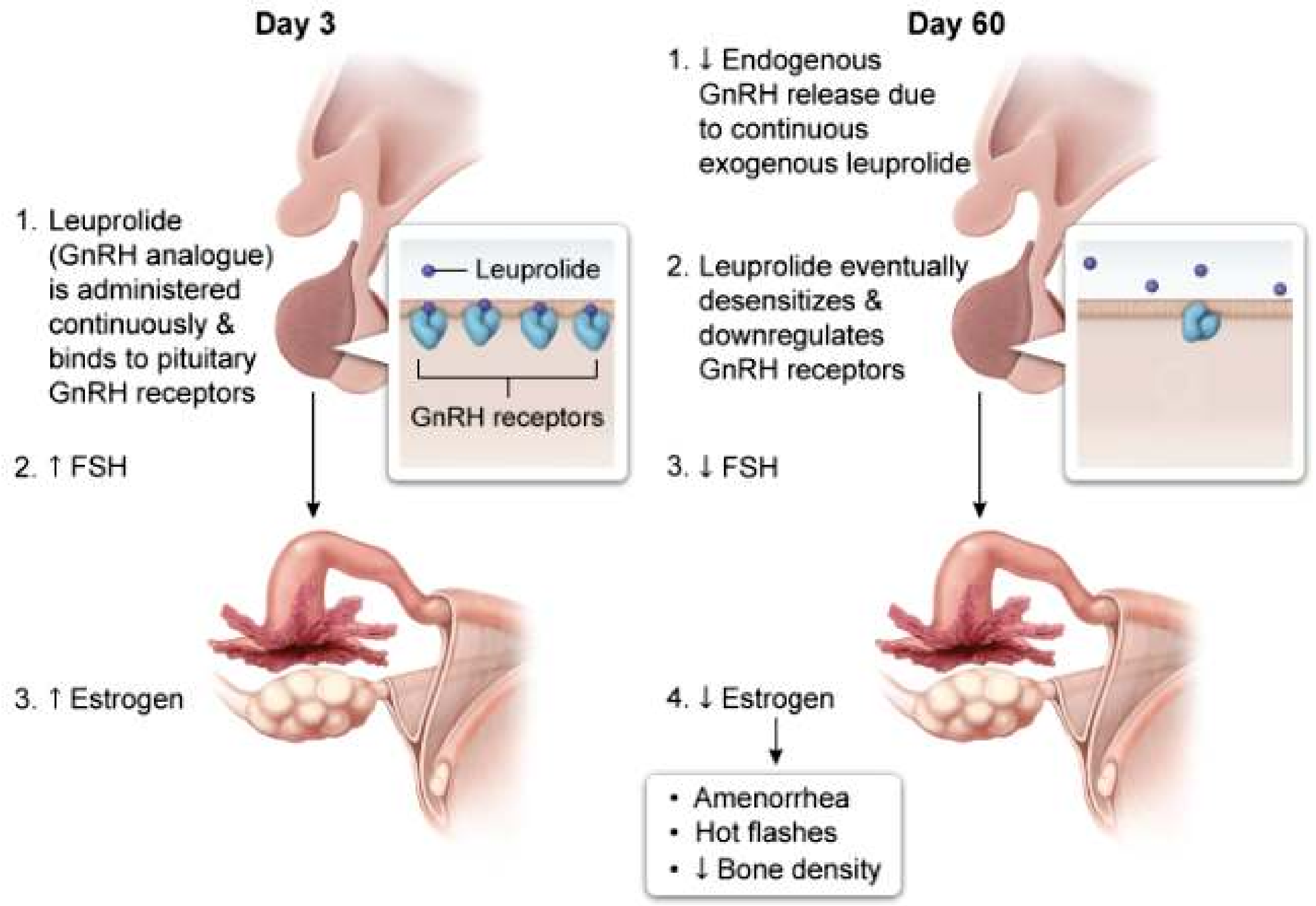
Effects of continuous leuprolide therapy over time


Day 3
1. Leuprolide (GnRH analogue) is administered continuously & binds to pituitary GnRH receptors
Leuprolide
GnRH receptors
2. ↑ FSH
3. ↑ Estrogen
Day 60
1. ↓ Endogenous GnRH release due to continuous exogenous leuprolide
2. Leuprolide eventually desensitizes & downregulates GnRH receptors
3. ↓ FSH
4. ↓ Estrogen
• Amenorrhea
• Hot flashes
• ↓ Bone density

	Day 3	Day 60
GnRH	Normal	↓
FSH	↑	↓
Estrogen	↑	↓

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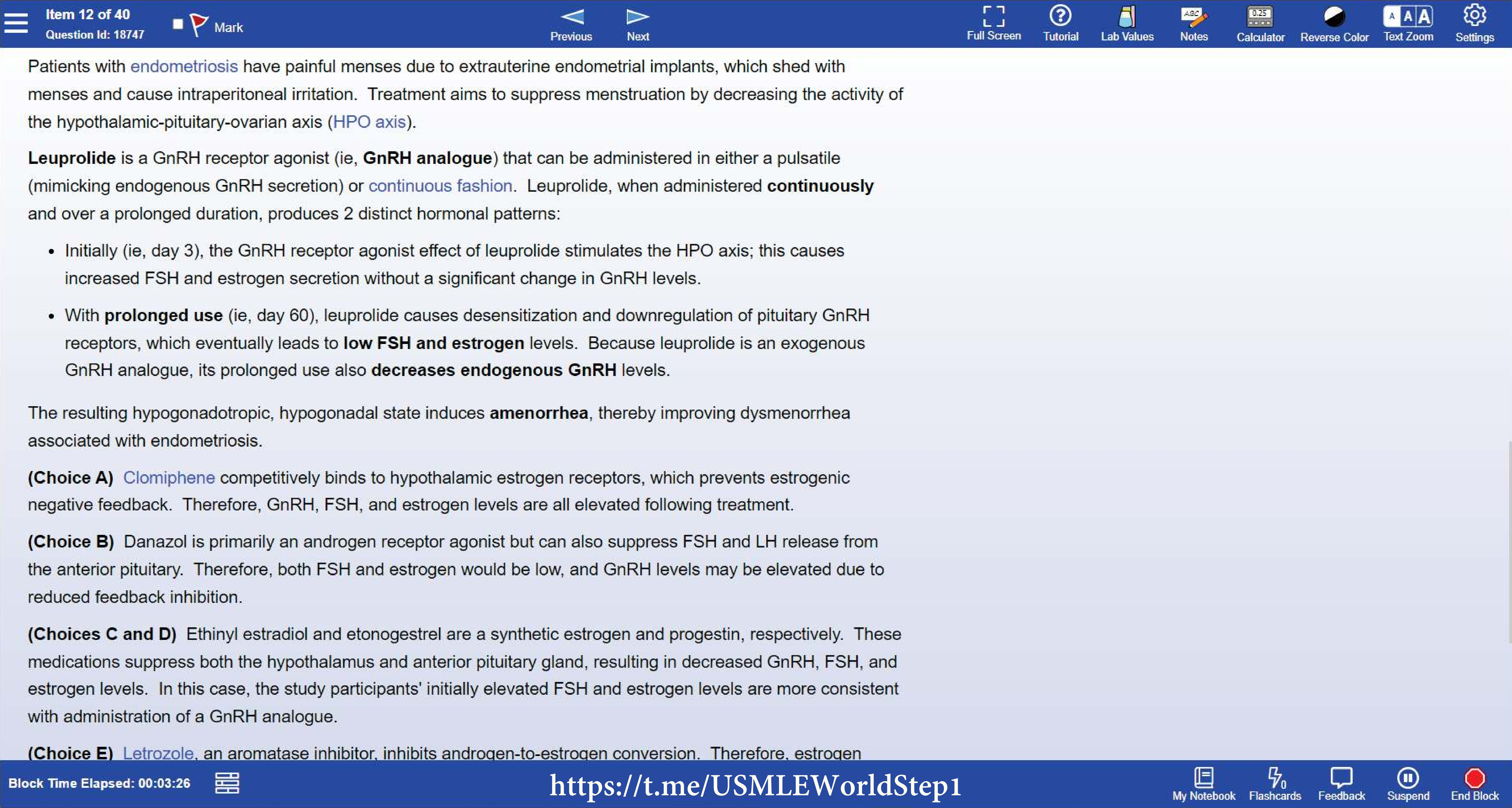
Patients with endometriosis have painful menses due to extrauterine endometrial implants, which shed with menses and cause intraperitoneal irritation. Treatment aims to suppress menstruation by decreasing the activity of



Patients with endometriosis have painful menses due to extrauterine endometrial implants, which shed with menses and cause intraperitoneal irritation. Treatment aims to suppress menstruation by decreasing the activity of the hypothalamic-pituitary-ovarian axis (HPO axis).

Leuprolide is a GnRH receptor agonist (ie, **GnRH analogue**) that can be administered in either a pulsatile (mimicking endogenous GnRH secretion) or continuous fashion. Leuprolide, when administered **continuously** and over a prolonged duration, produces 2 distinct hormonal patterns:

- Initially (ie, day 3), the GnRH receptor agonist effect of leuprolide stimulates the HPO axis; this causes increased FSH and estrogen secretion without a significant change in GnRH levels.
- With **prolonged use** (ie, day 60), leuprolide causes desensitization and downregulation of pituitary GnRH receptors, which eventually leads to **low FSH and estrogen** levels. Because leuprolide is an exogenous GnRH analogue, its prolonged use also **decreases endogenous GnRH** levels.

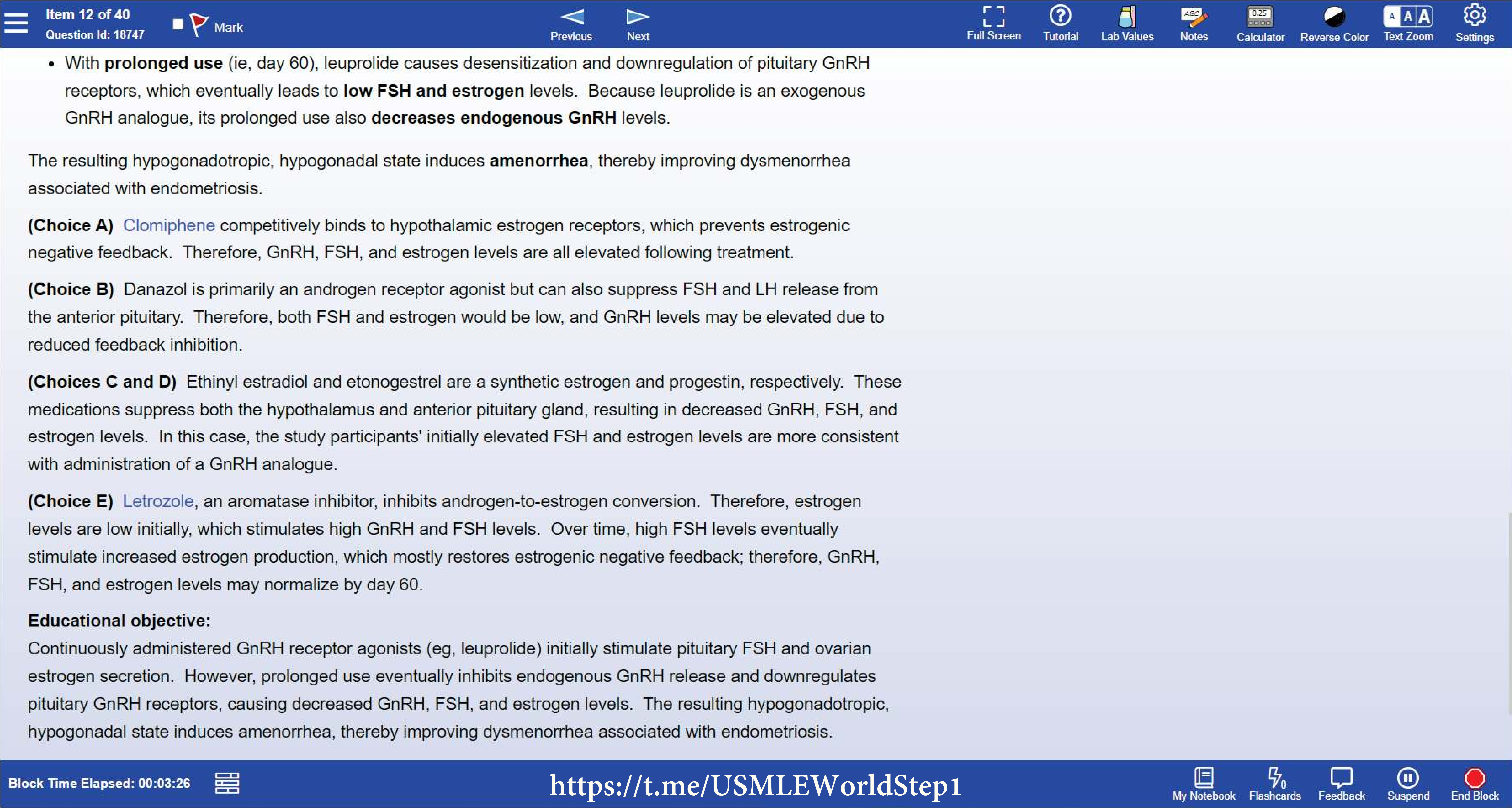
The resulting hypogonadotropic, hypogonadal state induces **amenorrhea**, thereby improving dysmenorrhea associated with endometriosis.

(Choice A) Clomiphene competitively binds to hypothalamic estrogen receptors, which prevents estrogenic negative feedback. Therefore, GnRH, FSH, and estrogen levels are all elevated following treatment.

(Choice B) Danazol is primarily an androgen receptor agonist but can also suppress FSH and LH release from the anterior pituitary. Therefore, both FSH and estrogen would be low, and GnRH levels may be elevated due to reduced feedback inhibition.

(Choices C and D) Ethinyl estradiol and etonogestrel are a synthetic estrogen and progestin, respectively. These medications suppress both the hypothalamus and anterior pituitary gland, resulting in decreased GnRH, FSH, and estrogen levels. In this case, the study participants' initially elevated FSH and estrogen levels are more consistent with administration of a GnRH analogue.

(Choice E) Letrozole, an aromatase inhibitor, inhibits androgen-to-estrogen conversion. Therefore, estrogen



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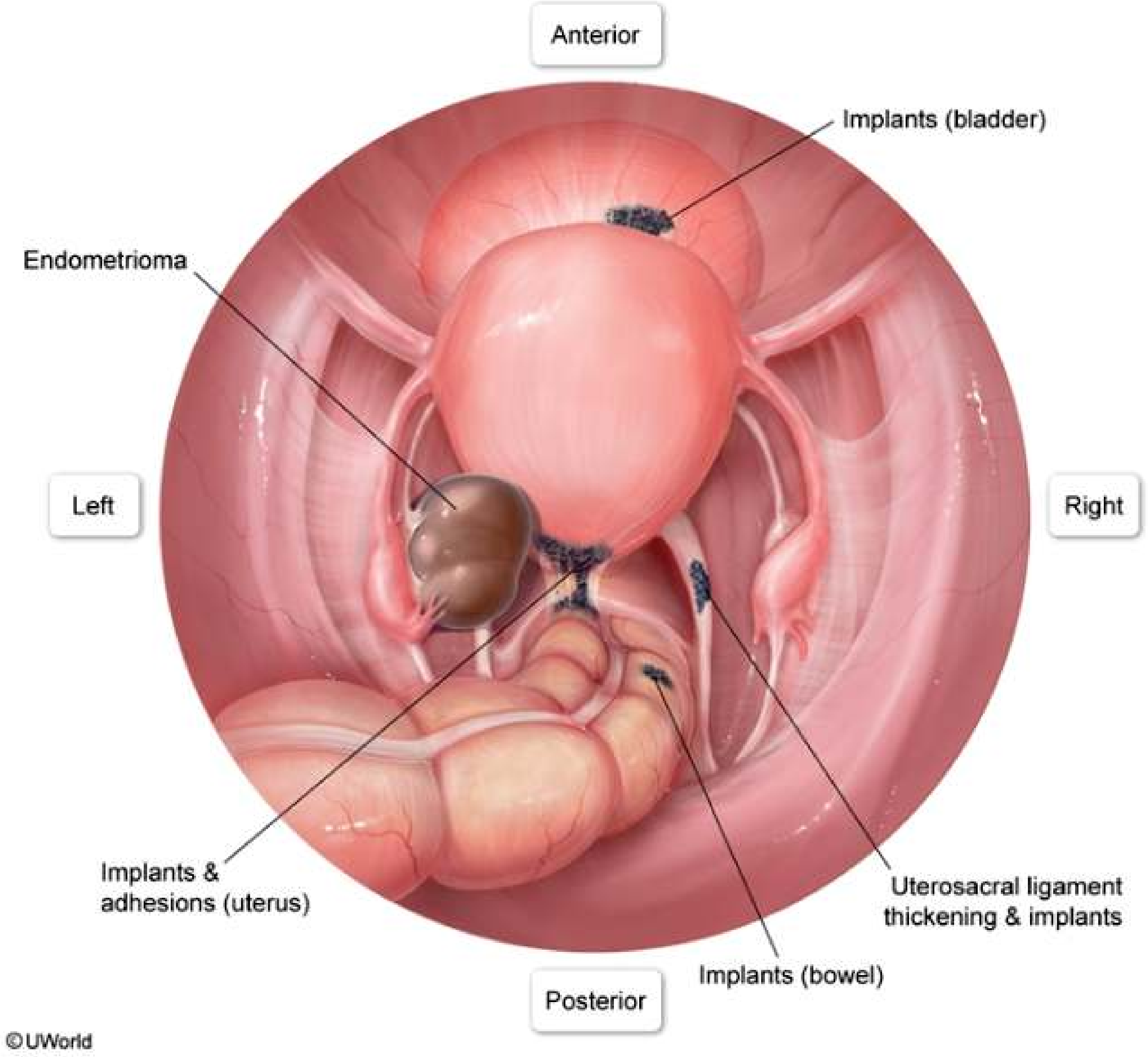
(Choice E) Letrozole, an aromatase inhibitor, inhibits androgen-to-estrogen conversion. Therefore, estrogen levels are low initially, which stimulates high GnRH and FSH levels. Over time, high FSH levels eventually stimulate increased estrogen production, which mostly restores estrogenic negative feedback; therefore, GnRH, FSH, and estrogen levels may normalize by day 60.

Educational objective:
Continuously administered GnRH receptor agonists (eg, leuprolide) initially stimulate pituitary FSH and ovarian estrogen secretion. However, prolonged use eventually inhibits endogenous GnRH release and downregulates pituitary GnRH receptors, causing decreased GnRH, FSH, and estrogen levels. The resulting hypogonadotropic, hypogonadal state induces amenorrhea, thereby improving dysmenorrhea associated with endometriosis.

- ↓ Bone density

Exhibit Display

Pelvic endometriosis


Anterior
Implants (bladder)
Endometrioma
Left
Right
Implants & adhesions (uterus)
Uterosacral ligament thickening & implants
Implants (bowel)
Posterior

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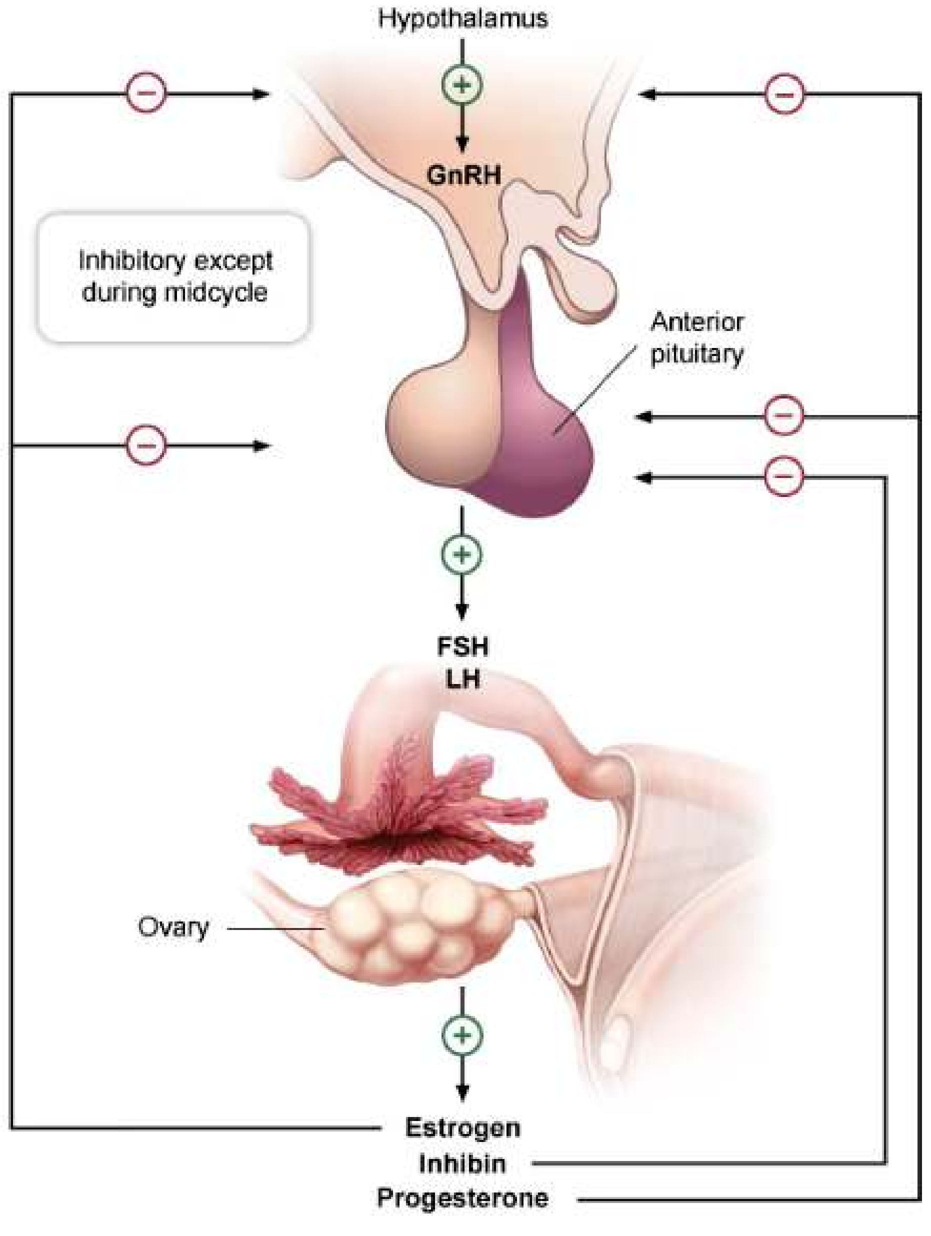
Hypothalamic-pituitary-ovarian axis


Hypothalamus
GnRH
Inhibitory except during midcycle
Anterior pituitary
FSH
LH
Ovary
Estrogen
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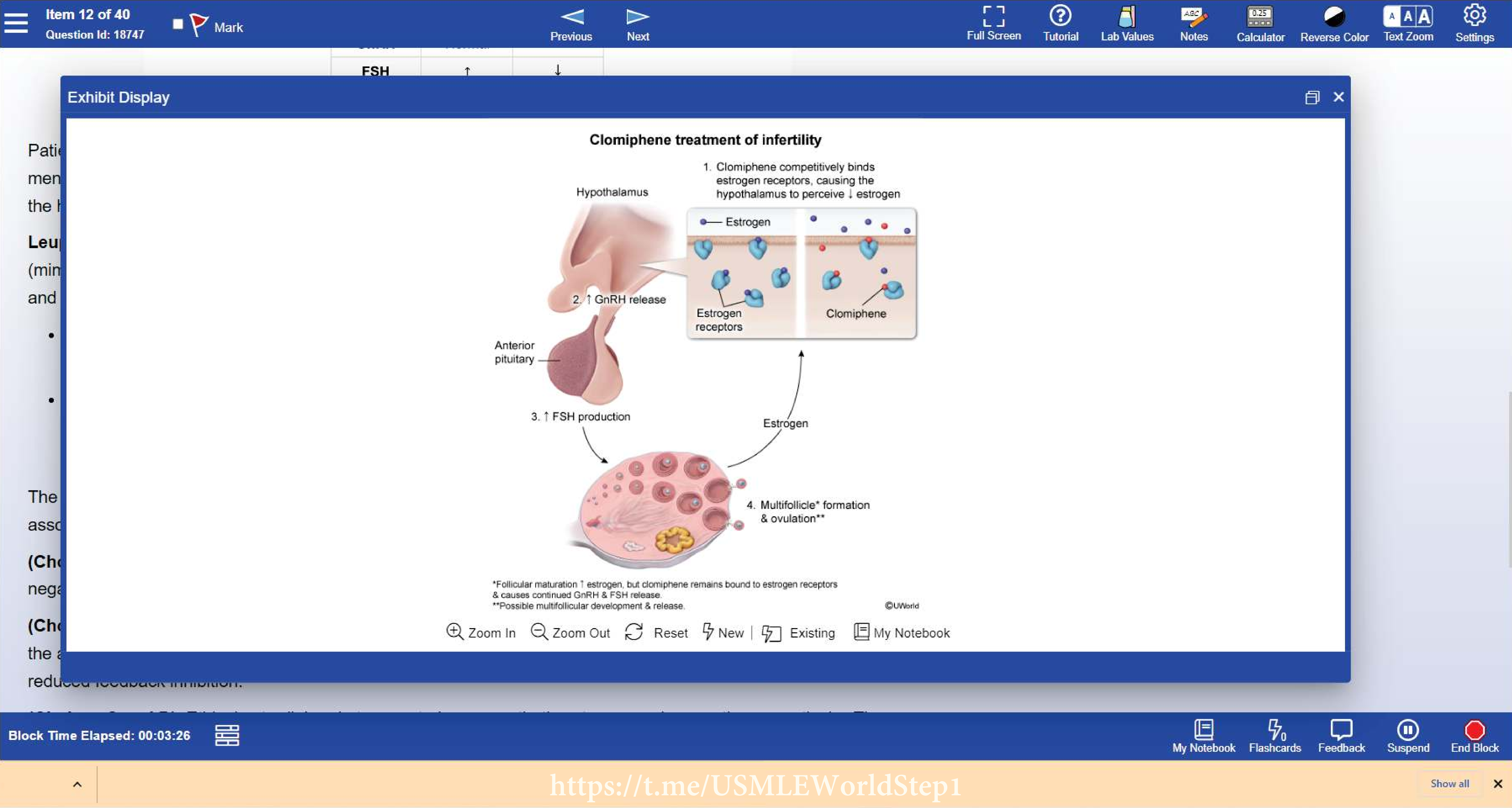
Item 12 of 40
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FSH
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Estrogen
Estrogen receptors
Clomiphene
2. ↑ GnRH release
Anterior pituitary
3. ↑ FSH production
Estrogen
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Clomiphene treatment of infertility

1. Clomiphene competitively binds estrogen receptors, causing the hypothalamus to perceive ↓ estrogen

4. Multifollicle* formation & ovulation**

*Follicular maturation ↑ estrogen, but clomiphene remains bound to estrogen receptors & causes continued GnRH & FSH release.
**Possible multifollicular development & release.

- With **prolonged use** (ie, day 60), leuprolide causes desensitization and downregulation of pituitary GnRH

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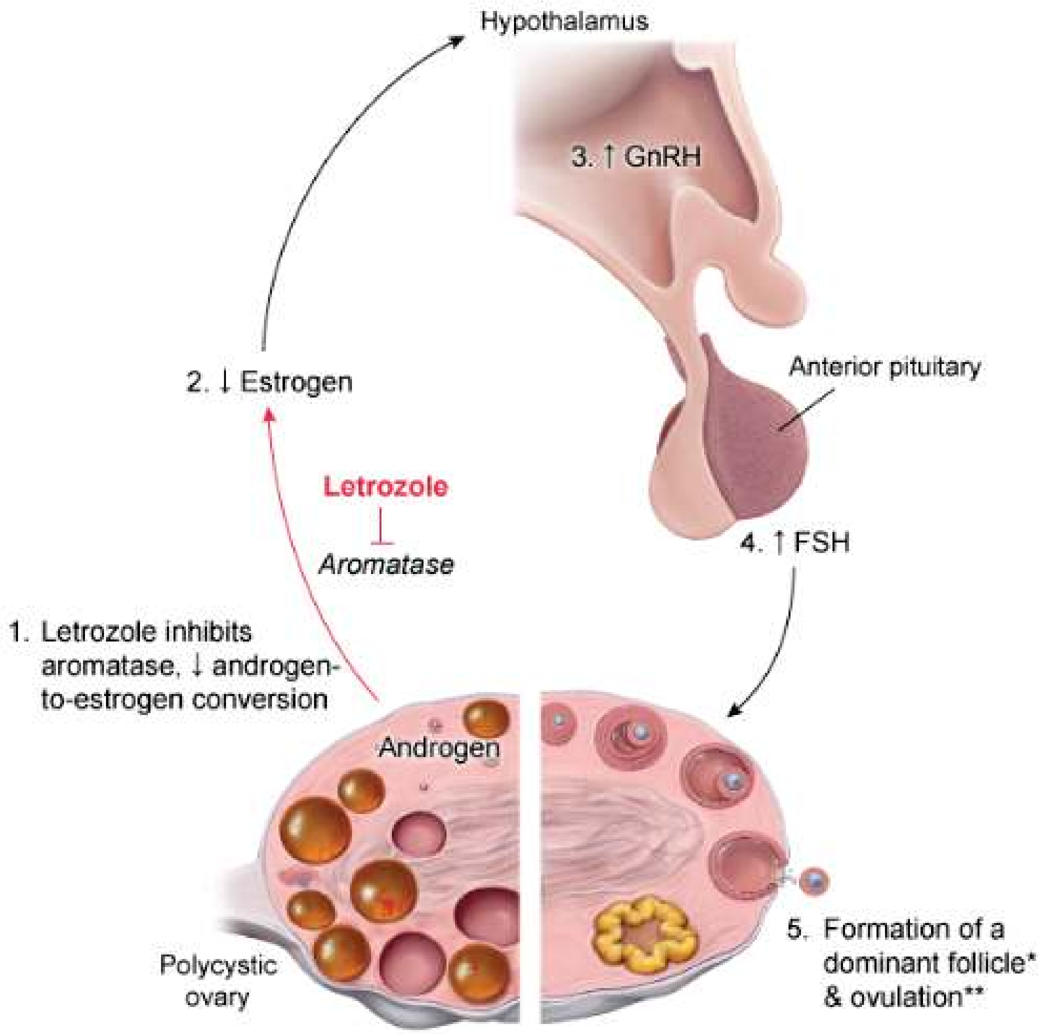
Letrozole treatment of infertility


Hypothalamus
3. ↑ GnRH
2. ↓ Estrogen
Anterior pituitary
Letrozole
Aromatase
4. ↑ FSH
1. Letrozole inhibits aromatase, ↓ androgen-to-estrogen conversion
Androgen
Polycystic ovary
5. Formation of a dominant follicle* & ovulation**

*Follicular formation ↑ estrogen, which restores estrogenic negative feedback & normalizes GnRH & FSH.
**Typically 1 follicle undergoes development & release.

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pituitary GnRH receptors, causing decreased GnRH, FSH, and estrogen levels. The resulting hypogonadotropic,

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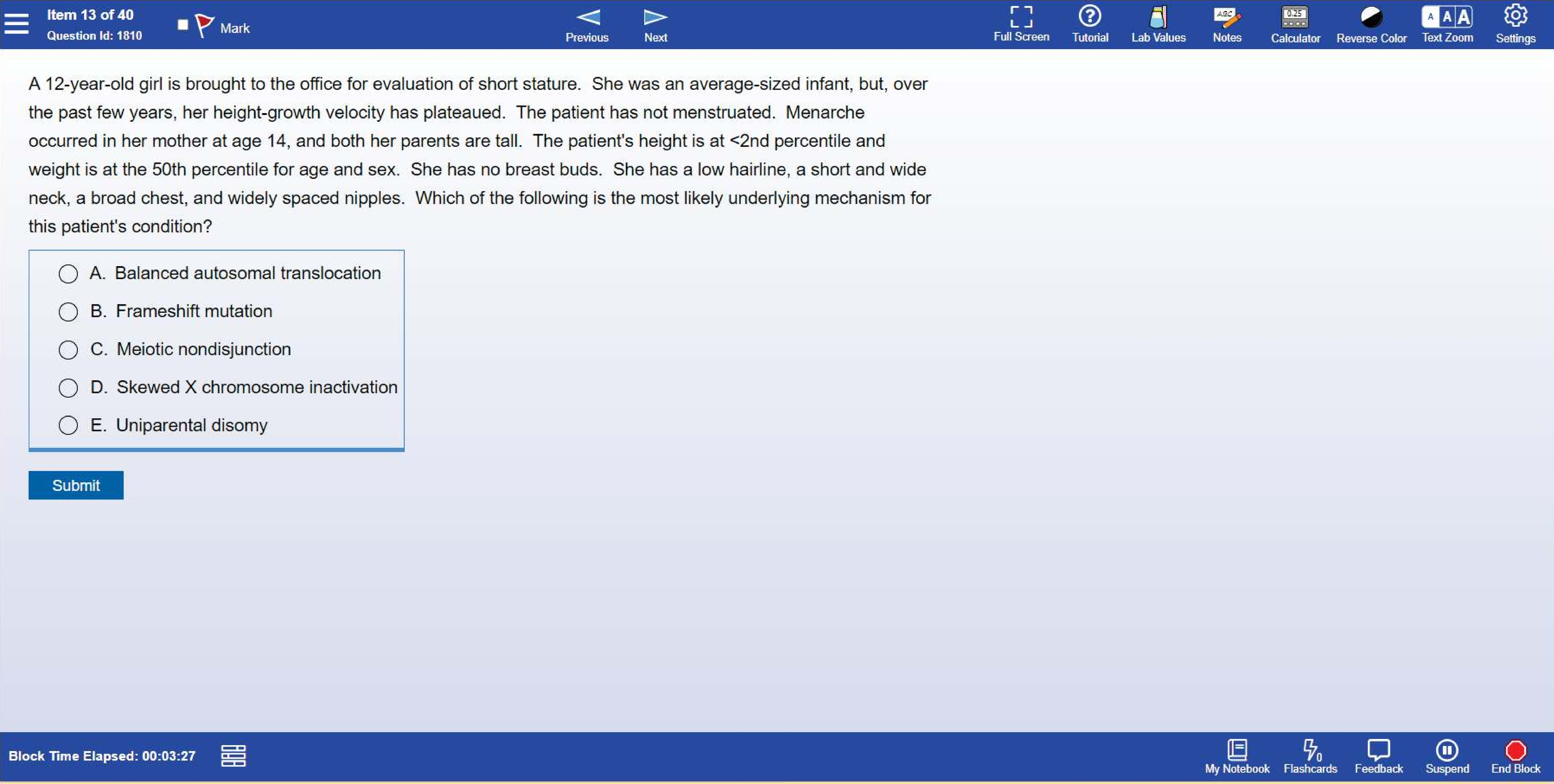
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A 12-year-old girl is brought to the office for evaluation of short stature. She was an average-sized infant, but, over the past few years, her height-growth velocity has plateaued. The patient has not menstruated. Menarche occurred in her mother at age 14, and both her parents are tall. The patient's height is at <2nd percentile and weight is at the 50th percentile for age and sex. She has no breast buds. She has a low hairline, a short and wide neck, a broad chest, and widely spaced nipples. Which of the following is the most likely underlying mechanism for this patient's condition?

○ A. Balanced autosomal translocation
○ B. Frameshift mutation
○ C. Meiotic nondisjunction
○ D. Skewed X chromosome inactivation
○ E. Uniparental disomy

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✓ ○ C. Meiotic nondisjunction
○ D. Skewed X chromosome inactivation
○ E. Uniparental disomy

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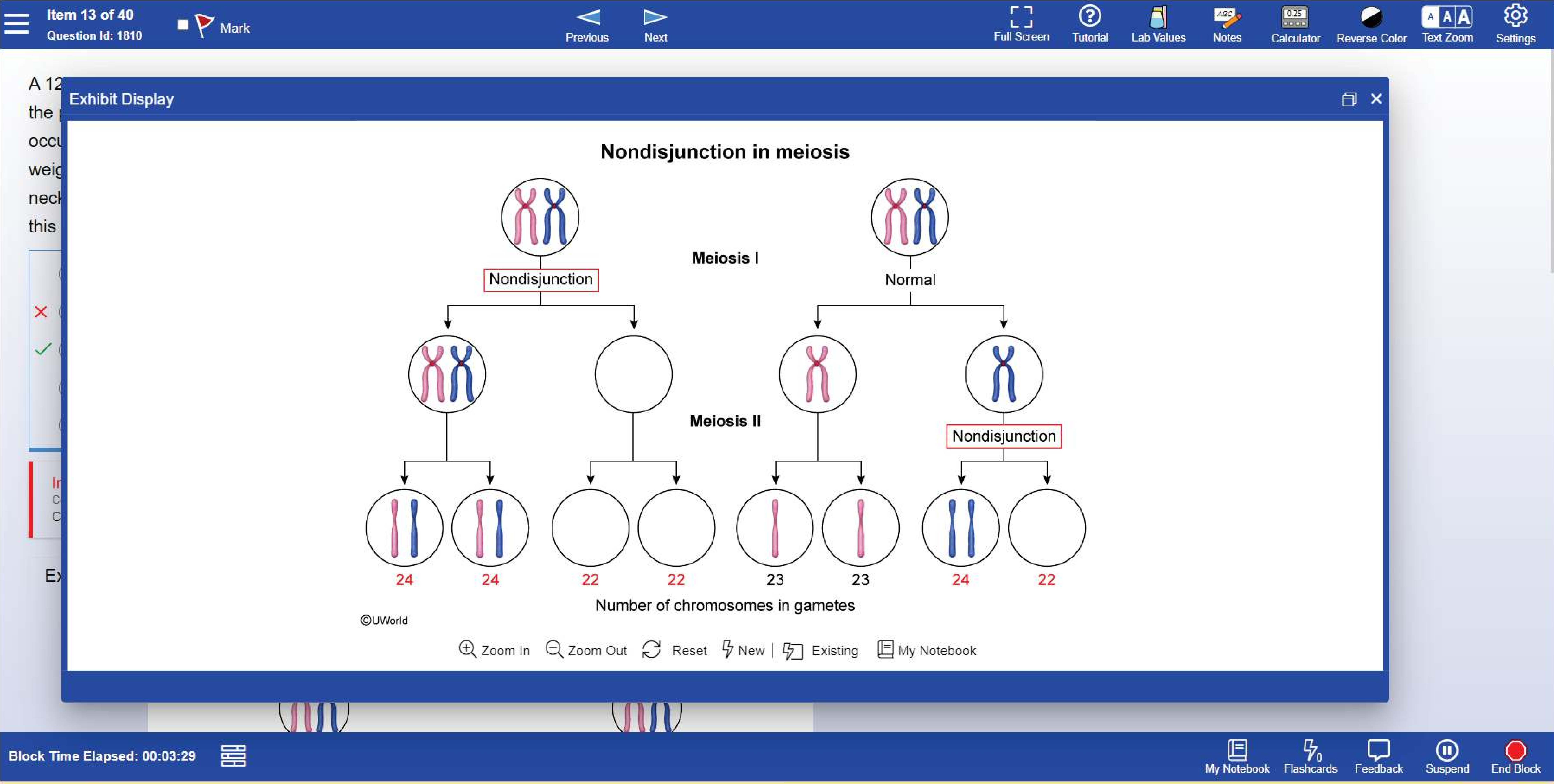
Explanation

Nondisjunction in meiosis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Nondisjunction in meiosis
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Nondisjunction
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Meiosis II
Nondisjunction
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Number of chromosomes in gametes
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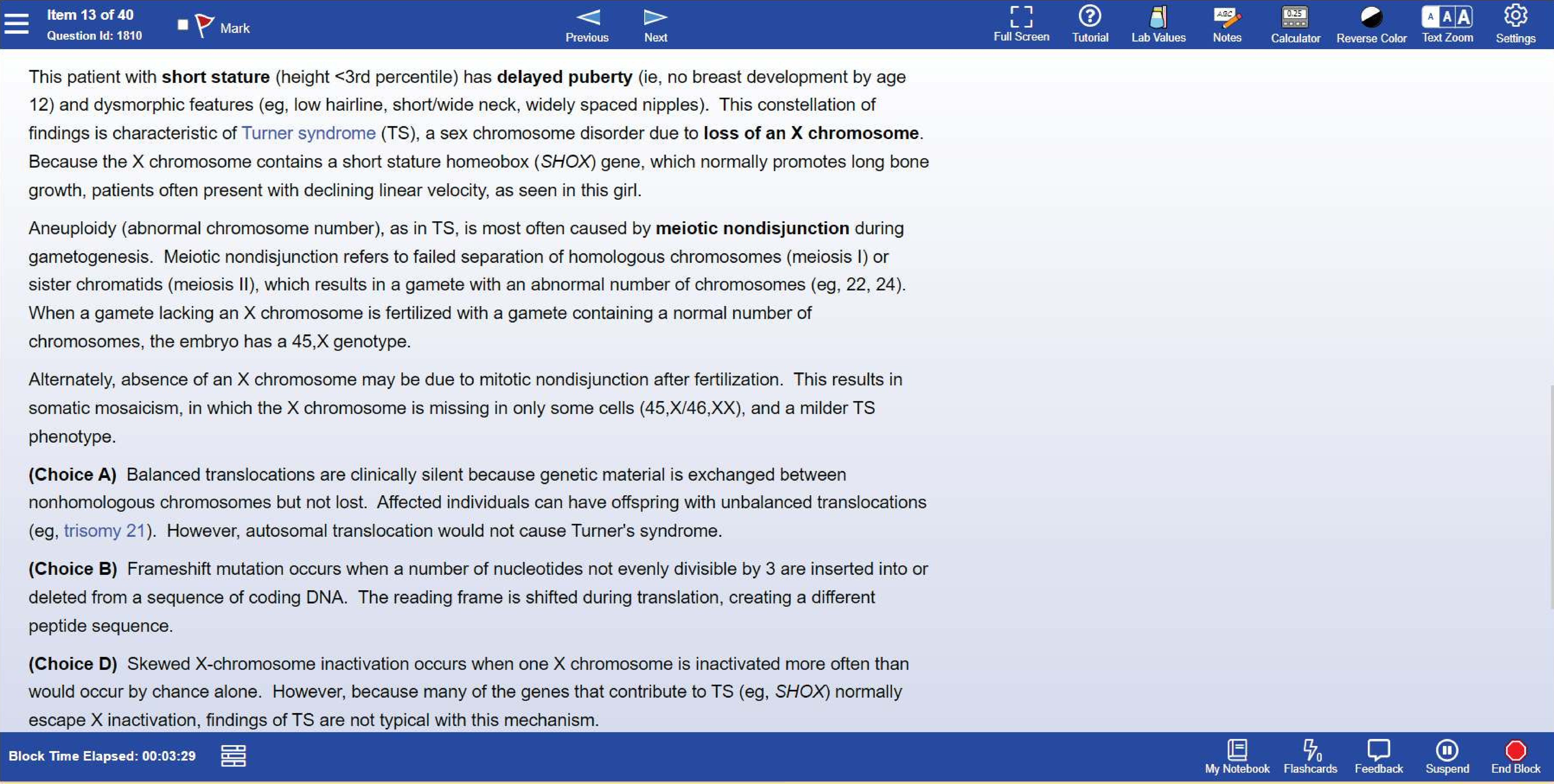


This patient with **short stature** (height <3rd percentile) has **delayed puberty** (ie, no breast development by age 12) and dysmorphic features (eg, low hairline, short/wide neck, widely spaced nipples). This constellation of findings is characteristic of Turner syndrome (TS), a sex chromosome disorder due to **loss of an X chromosome**. Because the X chromosome contains a short stature homeobox (*SHOX*) gene, which normally promotes long bone growth, patients often present with declining linear velocity, as seen in this girl.

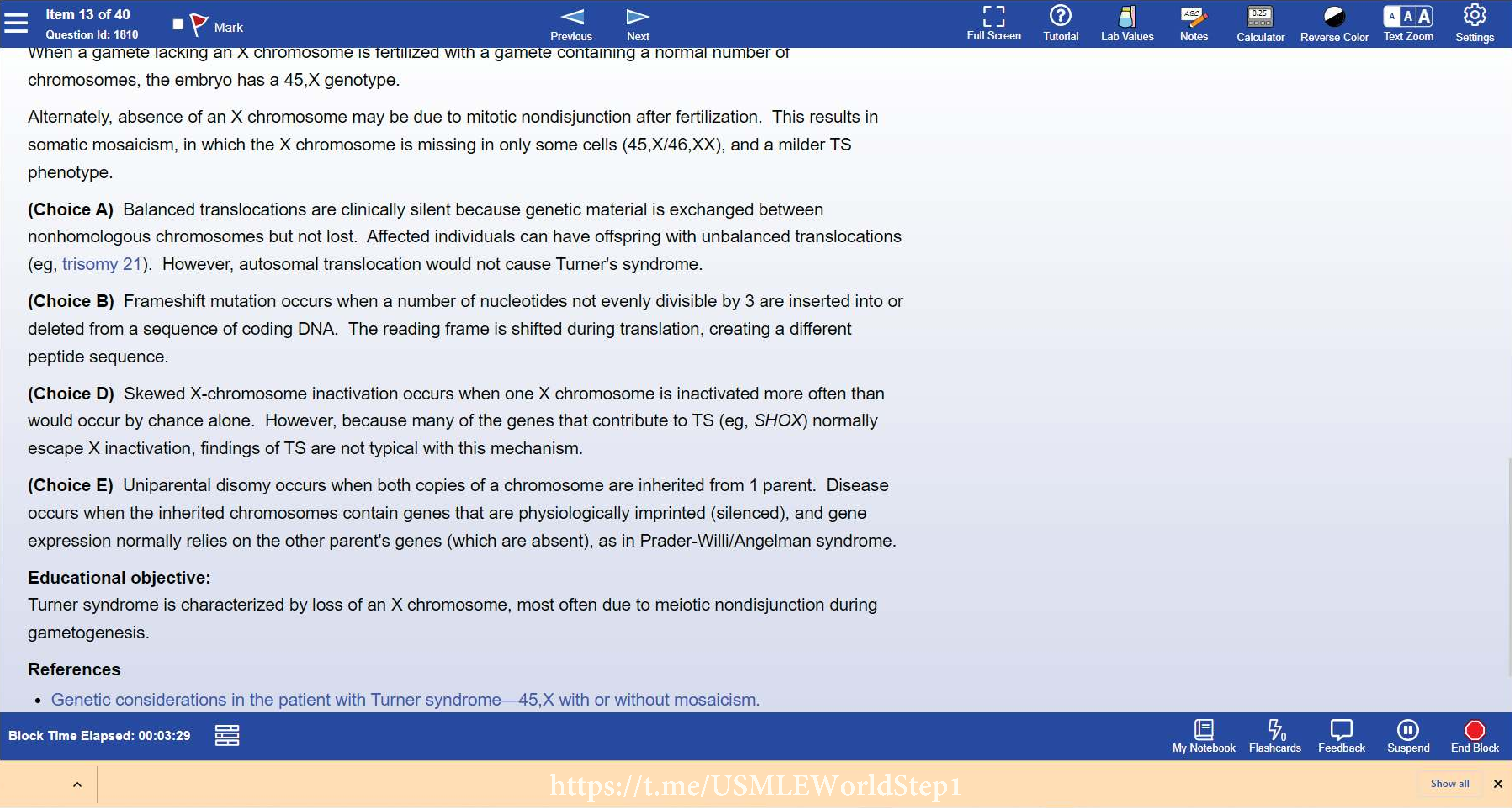
Aneuploidy (abnormal chromosome number), as in TS, is most often caused by **meiotic nondisjunction** during gametogenesis. Meiotic nondisjunction refers to failed separation of homologous chromosomes (meiosis I) or sister chromatids (meiosis II), which results in a gamete with an abnormal number of chromosomes (eg, 22, 24). When a gamete lacking an X chromosome is fertilized with a gamete containing a normal number of chromosomes, the embryo has a 45,X genotype.

Alternately, absence of an X chromosome may be due to mitotic nondisjunction after fertilization. This results in somatic mosaicism, in which the X chromosome is missing in only some cells (45,X/46,XX), and a milder TS phenotype.

(Choice A) Balanced translocations are clinically silent because genetic material is exchanged between nonhomologous chromosomes but not lost. Affected individuals can have offspring with unbalanced translocations (eg, trisomy 21). However, autosomal translocation would not cause Turner's syndrome.

(Choice B) Frameshift mutation occurs when a number of nucleotides not evenly divisible by 3 are inserted into or deleted from a sequence of coding DNA. The reading frame is shifted during translation, creating a different peptide sequence.

(Choice D) Skewed X-chromosome inactivation occurs when one X chromosome is inactivated more often than would occur by chance alone. However, because many of the genes that contribute to TS (eg, *SHOX*) normally escape X inactivation, findings of TS are not typical with this mechanism.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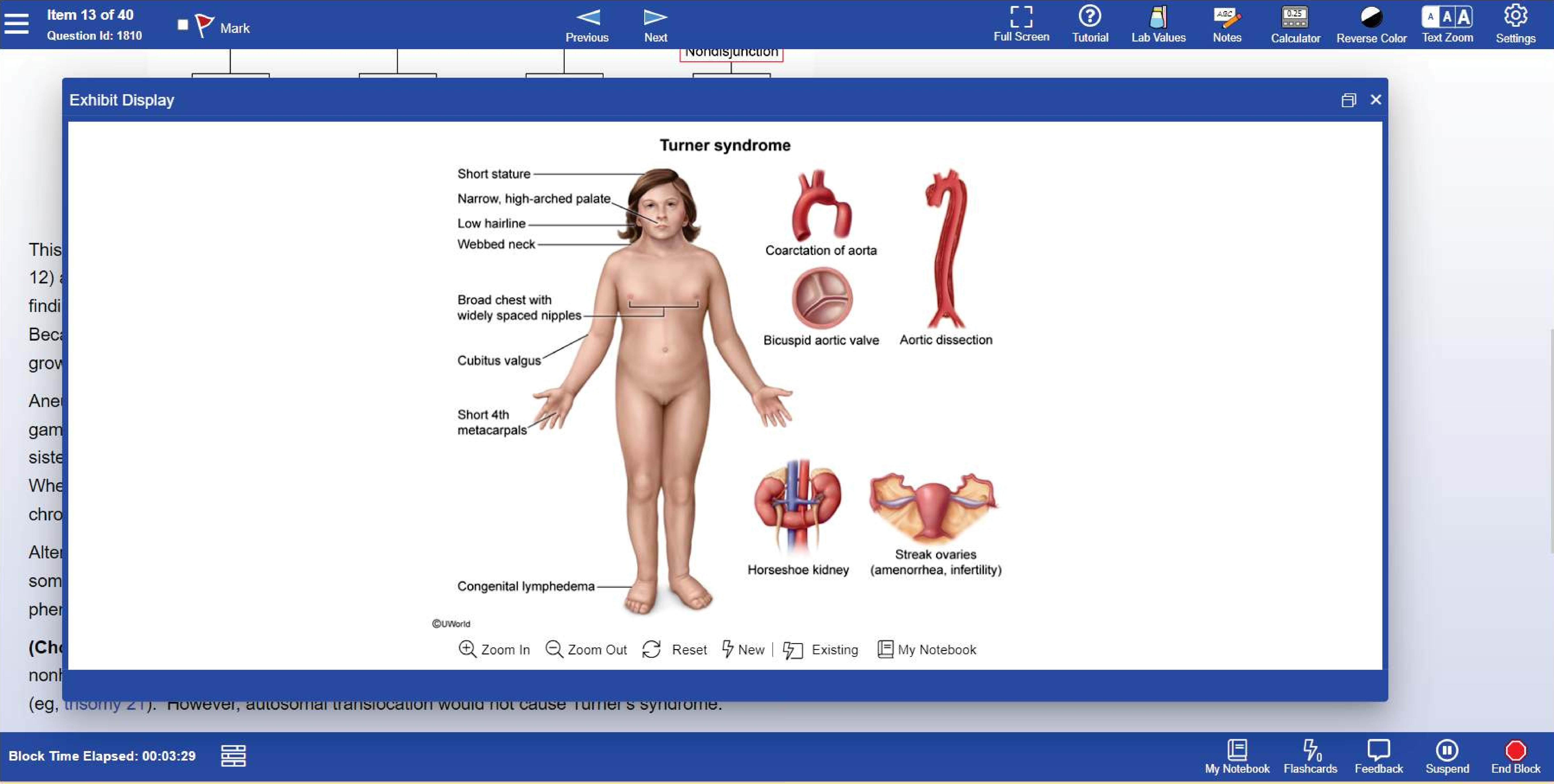
(Choice E) Uniparental disomy occurs when both copies of a chromosome are inherited from 1 parent. Disease occurs when the inherited chromosomes contain genes that are physiologically imprinted (silenced), and gene expression normally relies on the other parent's genes (which are absent), as in Prader-Willi/Angelman syndrome.

Educational objective:

Turner syndrome is characterized by loss of an X chromosome, most often due to meiotic nondisjunction during gametogenesis.

References

- Genetic considerations in the patient with Turner syndrome—45,X with or without mosaicism.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Nondisjunction
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Turner syndrome
Short stature
Narrow, high-arched palate
Low hairline
Webbed neck
Broad chest with widely spaced nipples
Cubitus valgus
Short 4th metacarpals
Congenital lymphedema
Coarctation of aorta
Bicuspid aortic valve
Aortic dissection
Horseshoe kidney
Streak ovaries (amenorrhea, infertility)
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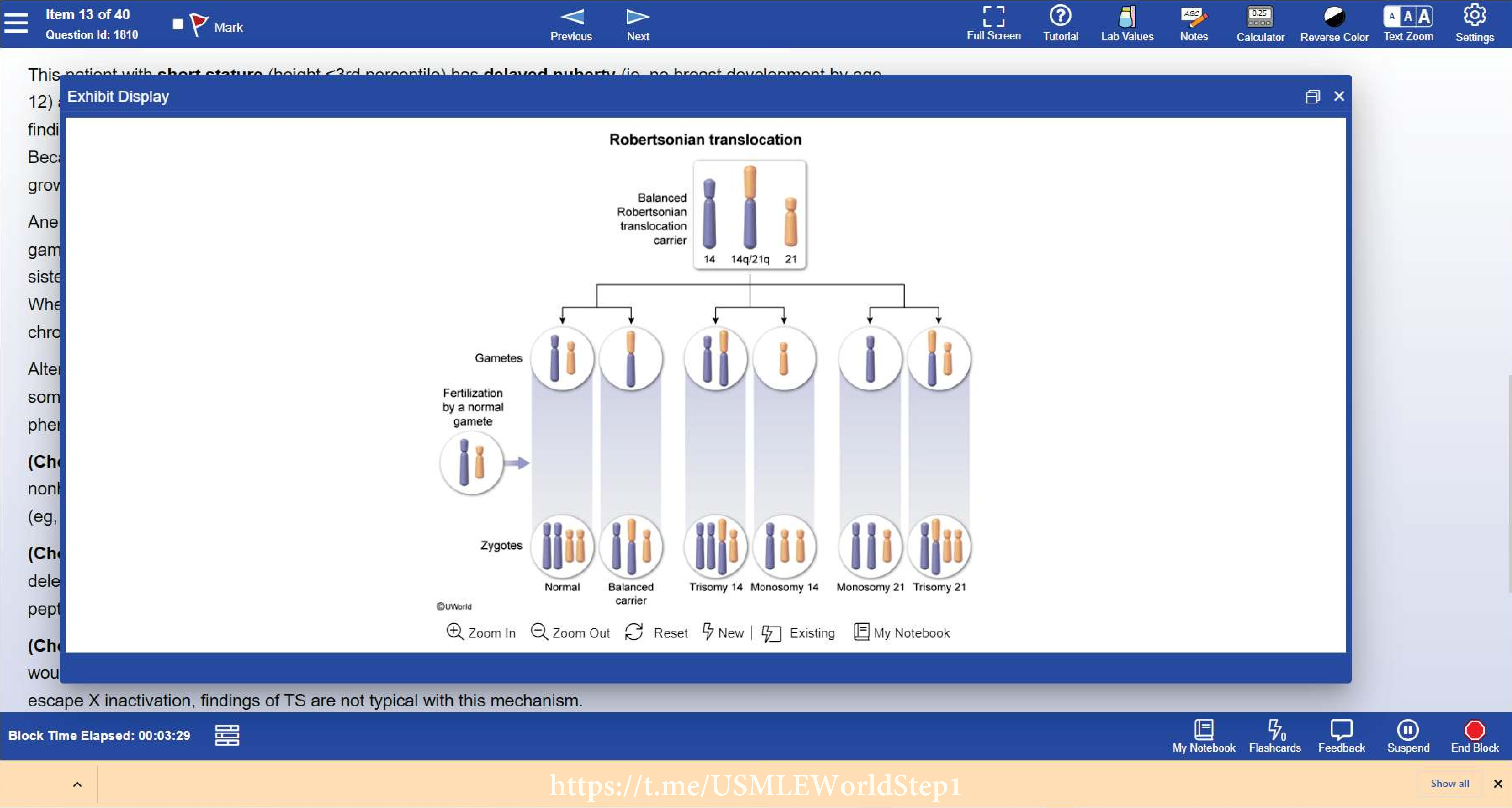
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This patient with **short stature** (height <3rd percentile) has **delayed puberty** (ie, no breast development by age

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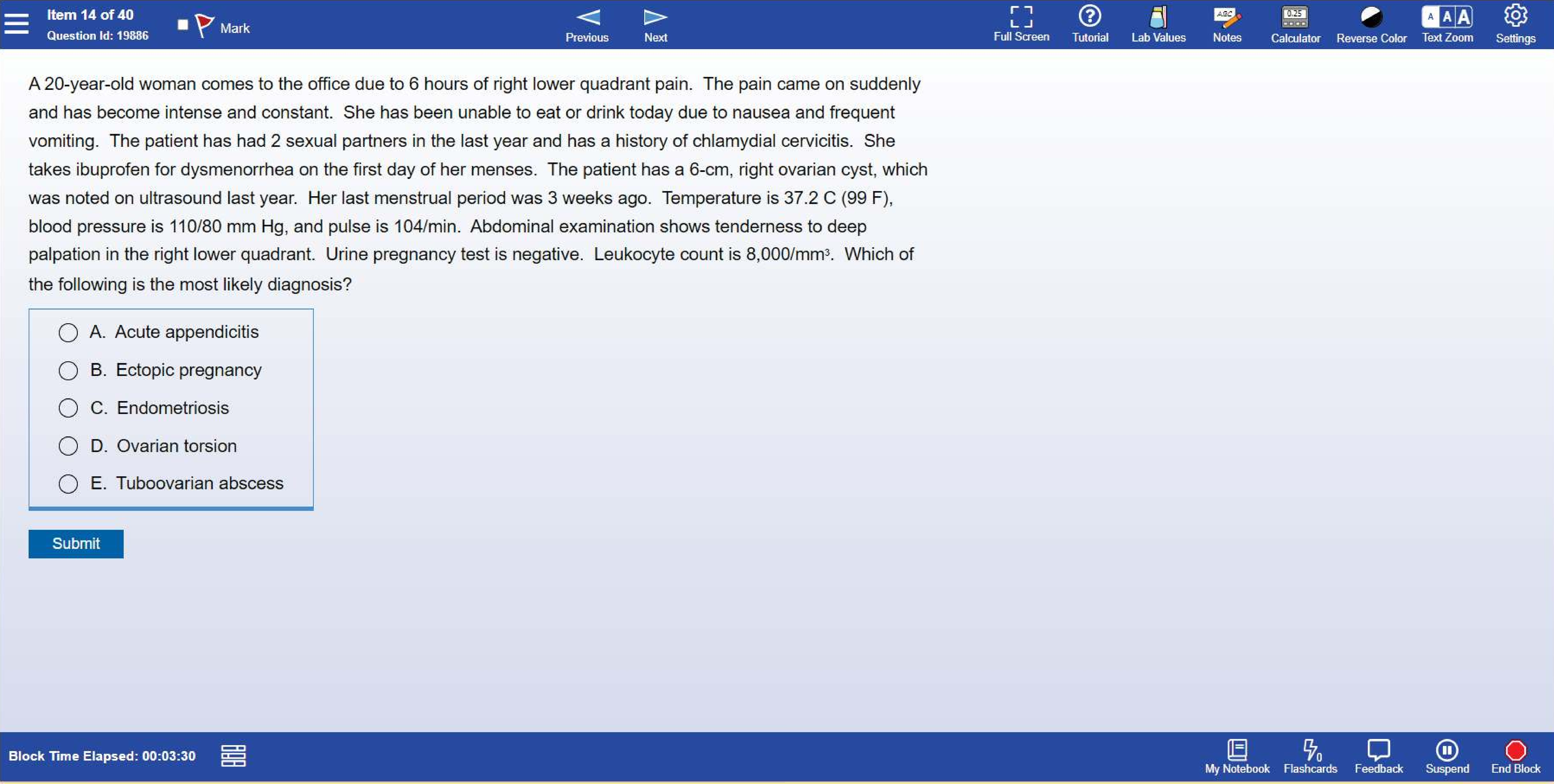
Item 14 of 40
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A 20-year-old woman comes to the office due to 6 hours of right lower quadrant pain. The pain came on suddenly and has become intense and constant. She has been unable to eat or drink today due to nausea and frequent vomiting. The patient has had 2 sexual partners in the last year and has a history of chlamydial cervicitis. She takes ibuprofen for dysmenorrhea on the first day of her menses. The patient has a 6-cm, right ovarian cyst, which was noted on ultrasound last year. Her last menstrual period was 3 weeks ago. Temperature is 37.2 C (99 F), blood pressure is 110/80 mm Hg, and pulse is 104/min. Abdominal examination shows tenderness to deep palpation in the right lower quadrant. Urine pregnancy test is negative. Leukocyte count is 8,000/mm^3. Which of the following is the most likely diagnosis?

○ A. Acute appendicitis
○ B. Ectopic pregnancy
○ C. Endometriosis
○ D. Ovarian torsion
○ E. Tuboovarian abscess

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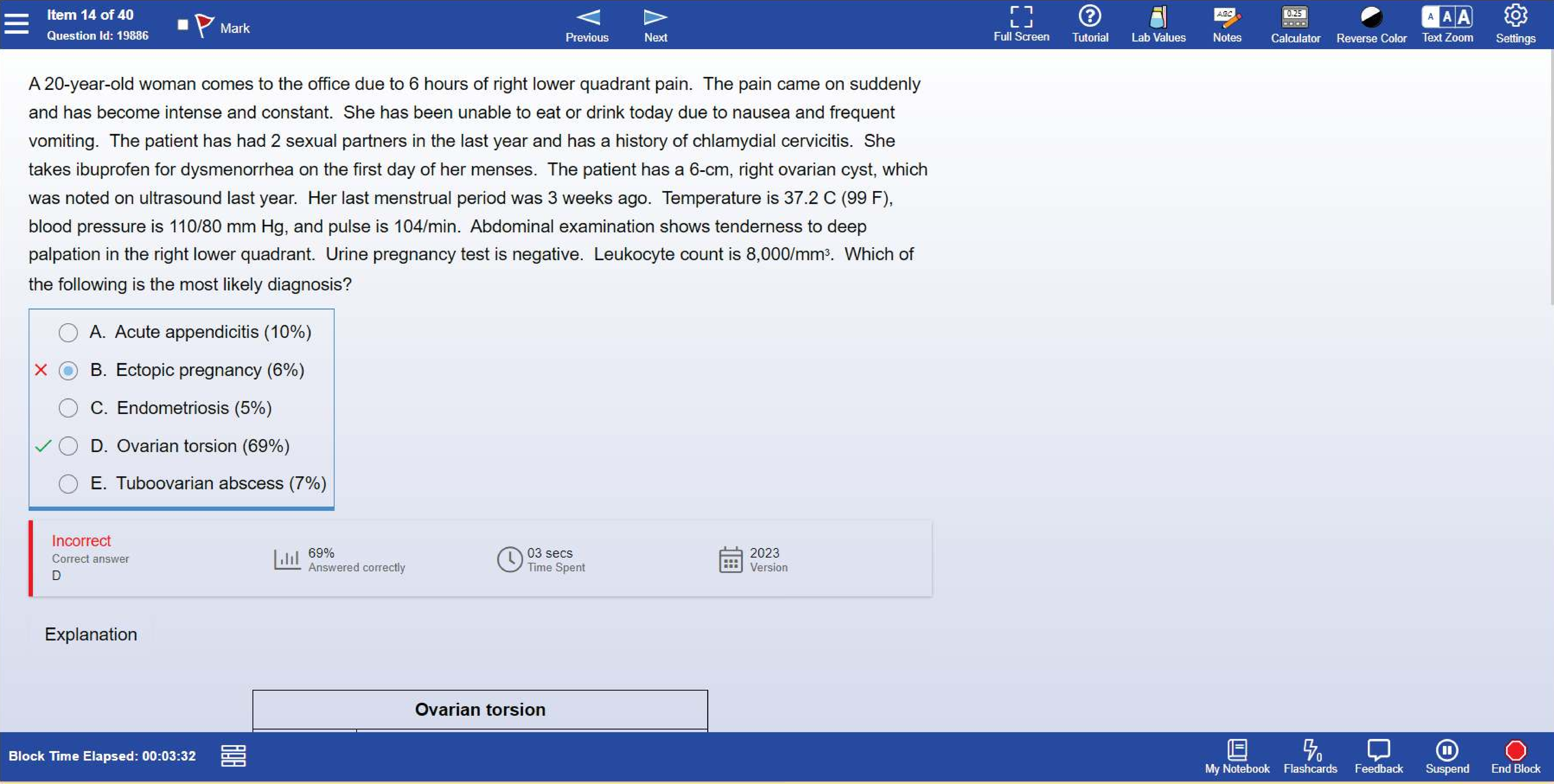
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Question Id: 19886
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- ○ A. Acute appendicitis (10%)
- ✗ ● B. Ectopic pregnancy (6%)
- ○ C. Endometriosis (5%)
- ✓ ○ D. Ovarian torsion (69%)
- ○ E. Tuboovarian abscess (7%)

Incorrect
Correct answer
D

69%
Answered correctly

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Explanation

Ovarian torsion

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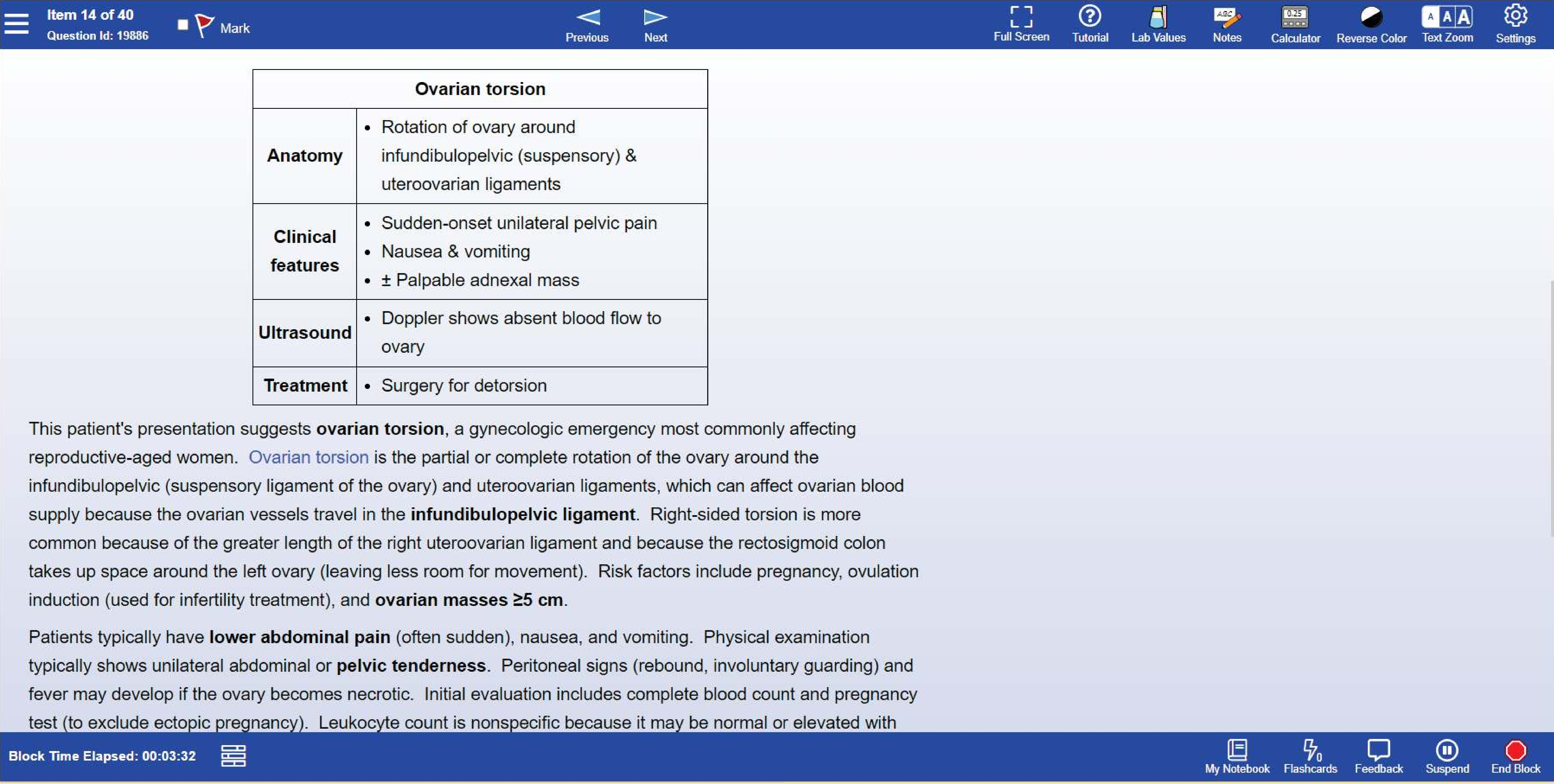
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Ovarian torsion	
Anatomy	• Rotation of ovary around infundibulopelvic (suspensory) & uteroovarian ligaments
Clinical features	• Sudden-onset unilateral pelvic pain • Nausea & vomiting • ± Palpable adnexal mass
Ultrasound	• Doppler shows absent blood flow to ovary
Treatment	• Surgery for detorsion

This patient's presentation suggests **ovarian torsion**, a gynecologic emergency most commonly affecting reproductive-aged women. Ovarian torsion is the partial or complete rotation of the ovary around the infundibulopelvic (suspensory ligament of the ovary) and uteroovarian ligaments, which can affect ovarian blood supply because the ovarian vessels travel in the **infundibulopelvic ligament**. Right-sided torsion is more common because of the greater length of the right uteroovarian ligament and because the rectosigmoid colon takes up space around the left ovary (leaving less room for movement). Risk factors include pregnancy, ovulation induction (used for infertility treatment), and **ovarian masses ≥5 cm**.

Patients typically have **lower abdominal pain** (often sudden), nausea, and vomiting. Physical examination typically shows unilateral abdominal or **pelvic tenderness**. Peritoneal signs (rebound, involuntary guarding) and fever may develop if the ovary becomes necrotic. Initial evaluation includes complete blood count and pregnancy test (to exclude ectopic pregnancy). Leukocyte count is nonspecific because it may be normal or elevated with

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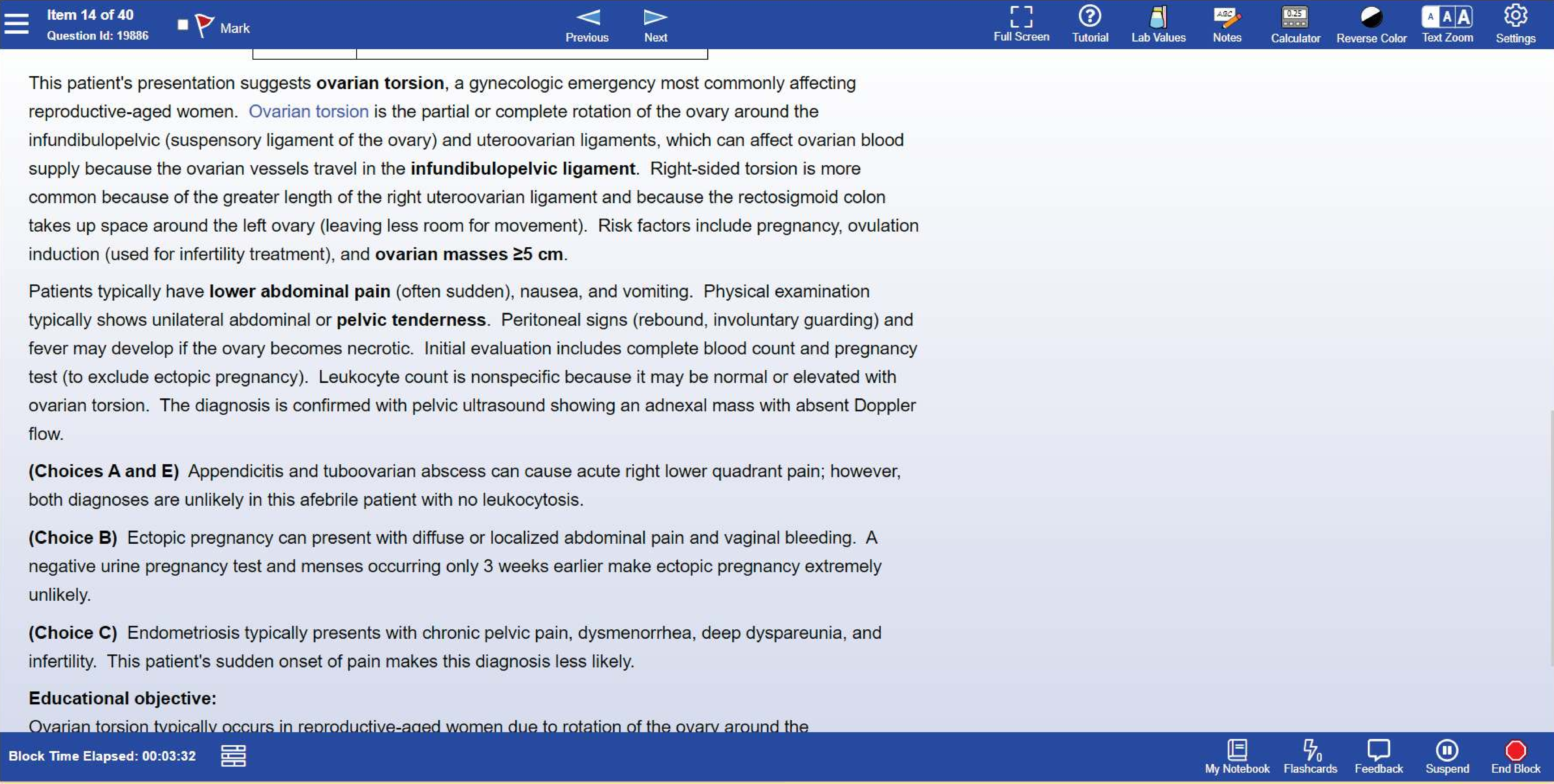

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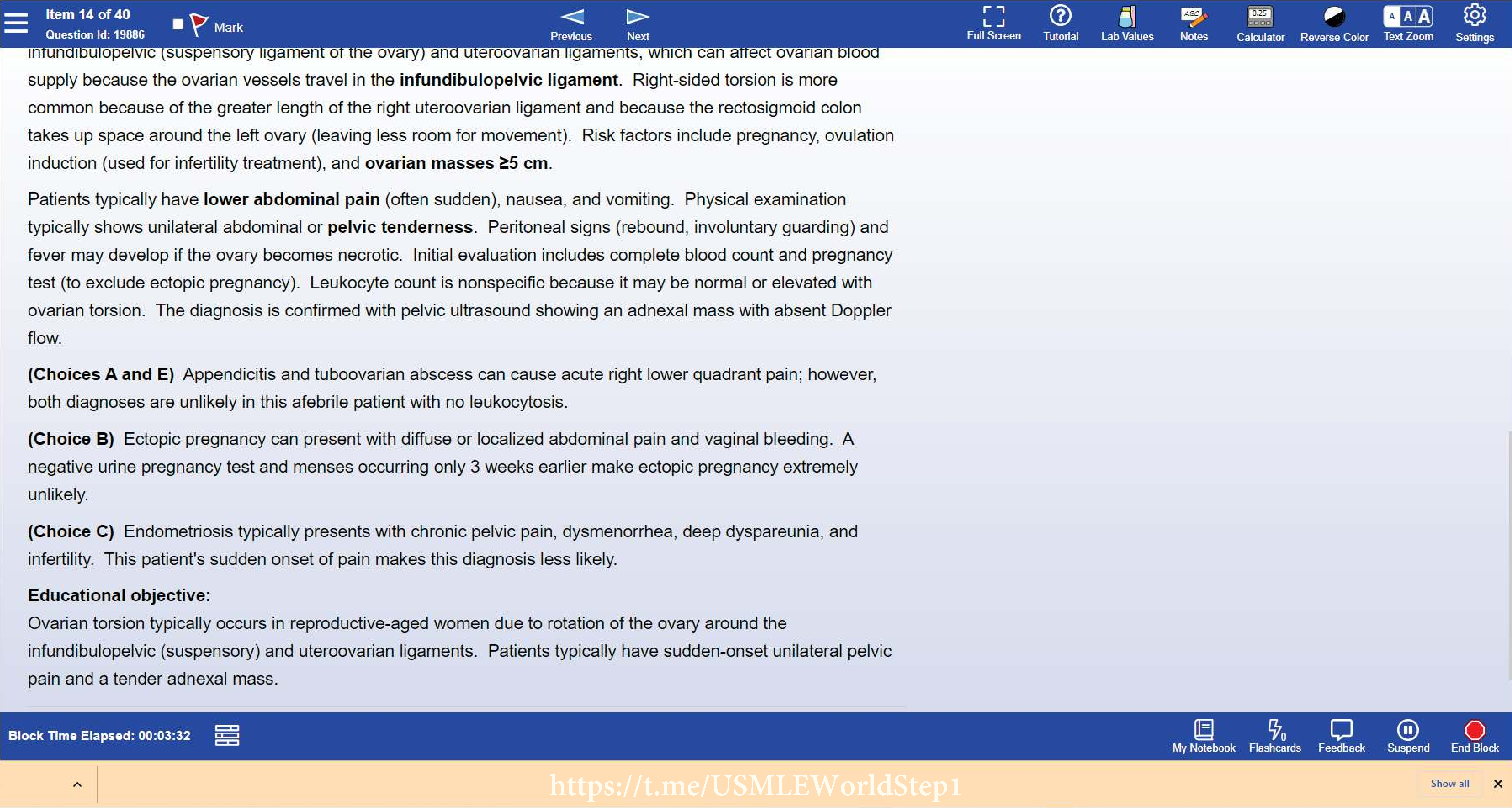
(Choices A and E) Appendicitis and tuboovarian abscess can cause acute right lower quadrant pain; however, both diagnoses are unlikely in this afebrile patient with no leukocytosis.

(Choice B) Ectopic pregnancy can present with diffuse or localized abdominal pain and vaginal bleeding. A negative urine pregnancy test and menses occurring only 3 weeks earlier make ectopic pregnancy extremely unlikely.

(Choice C) Endometriosis typically presents with chronic pelvic pain, dysmenorrhea, deep dyspareunia, and infertility. This patient's sudden onset of pain makes this diagnosis less likely.

Educational objective:

Ovarian torsion typically occurs in reproductive-aged women due to rotation of the ovary around the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Patients typically have **lower abdominal pain** (often sudden), nausea, and vomiting. Physical examination typically shows unilateral abdominal or **pelvic tenderness**. Peritoneal signs (rebound, involuntary guarding) and fever may develop if the ovary becomes necrotic. Initial evaluation includes complete blood count and pregnancy test (to exclude ectopic pregnancy). Leukocyte count is nonspecific because it may be normal or elevated with ovarian torsion. The diagnosis is confirmed with pelvic ultrasound showing an adnexal mass with absent Doppler flow.

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Educational objective:

Ovarian torsion typically occurs in reproductive-aged women due to rotation of the ovary around the infundibulopelvic (suspensory) and uteroovarian ligaments. Patients typically have sudden-onset unilateral pelvic pain and a tender adnexal mass.

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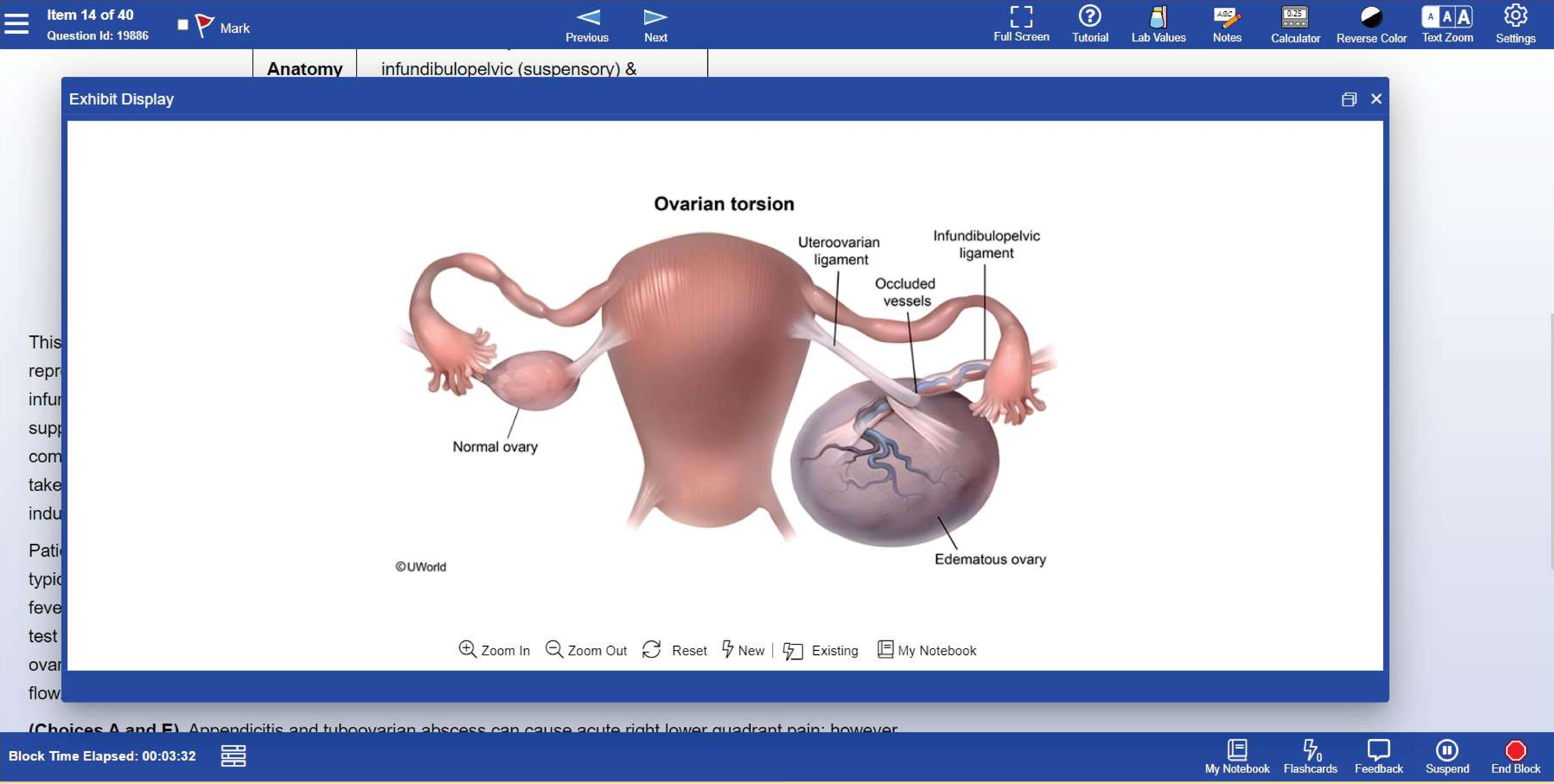
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Uteroovarian ligament
Infundibulopelvic ligament
Occluded vessels
Normal ovary
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Ovarian torsion

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(Choices A and E) Appendicitis and tuboovarian abscess can cause acute right lower quadrant pain; however

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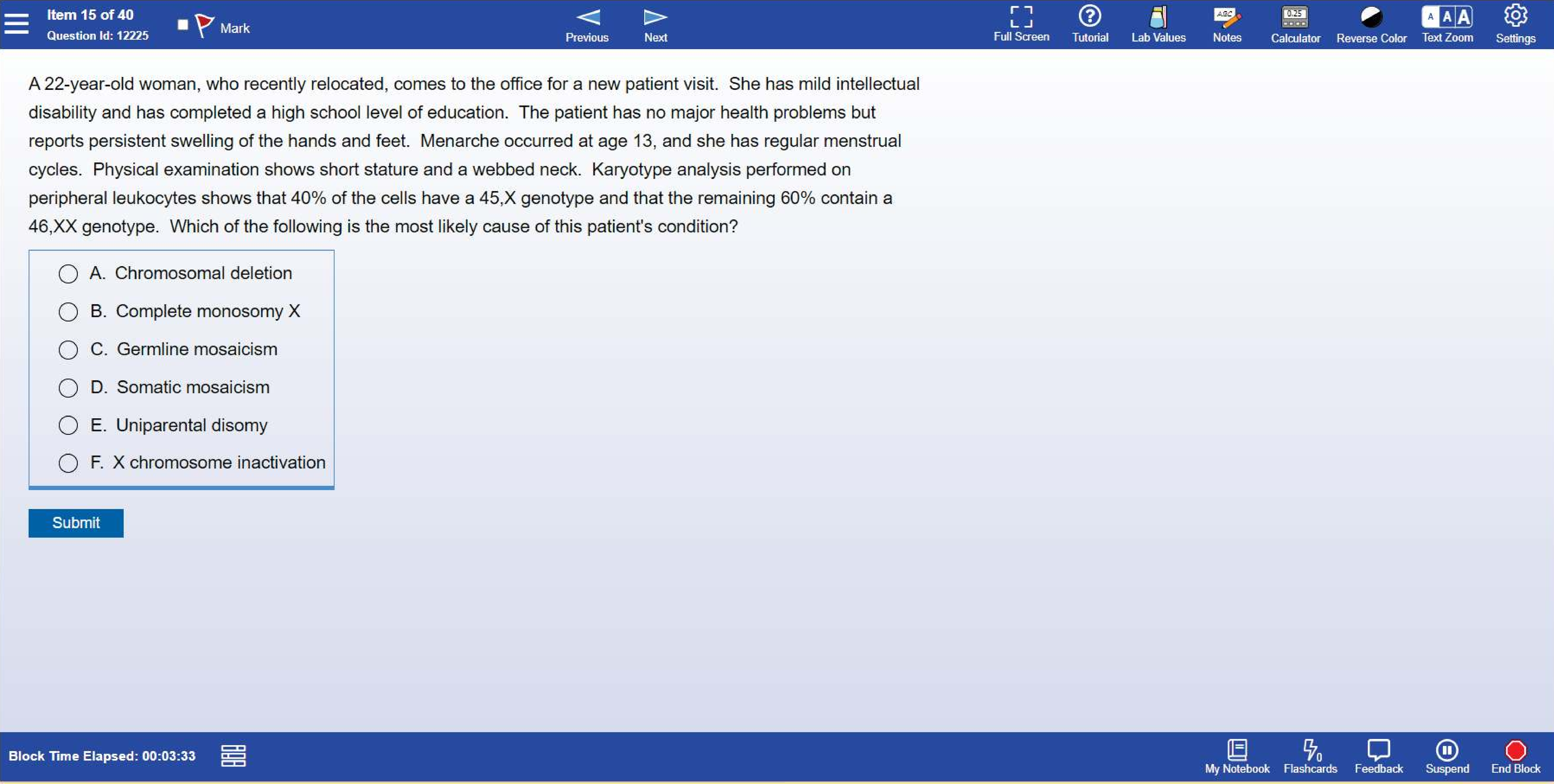
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Question Id: 12225
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A 22-year-old woman, who recently relocated, comes to the office for a new patient visit. She has mild intellectual disability and has completed a high school level of education. The patient has no major health problems but reports persistent swelling of the hands and feet. Menarche occurred at age 13, and she has regular menstrual cycles. Physical examination shows short stature and a webbed neck. Karyotype analysis performed on peripheral leukocytes shows that 40% of the cells have a 45,X genotype and that the remaining 60% contain a 46,XX genotype. Which of the following is the most likely cause of this patient's condition?

- ○ A. Chromosomal deletion
- ○ B. Complete monosomy X
- ○ C. Germline mosaicism
- ○ D. Somatic mosaicism
- ○ E. Uniparental disomy
- ○ F. X chromosome inactivation

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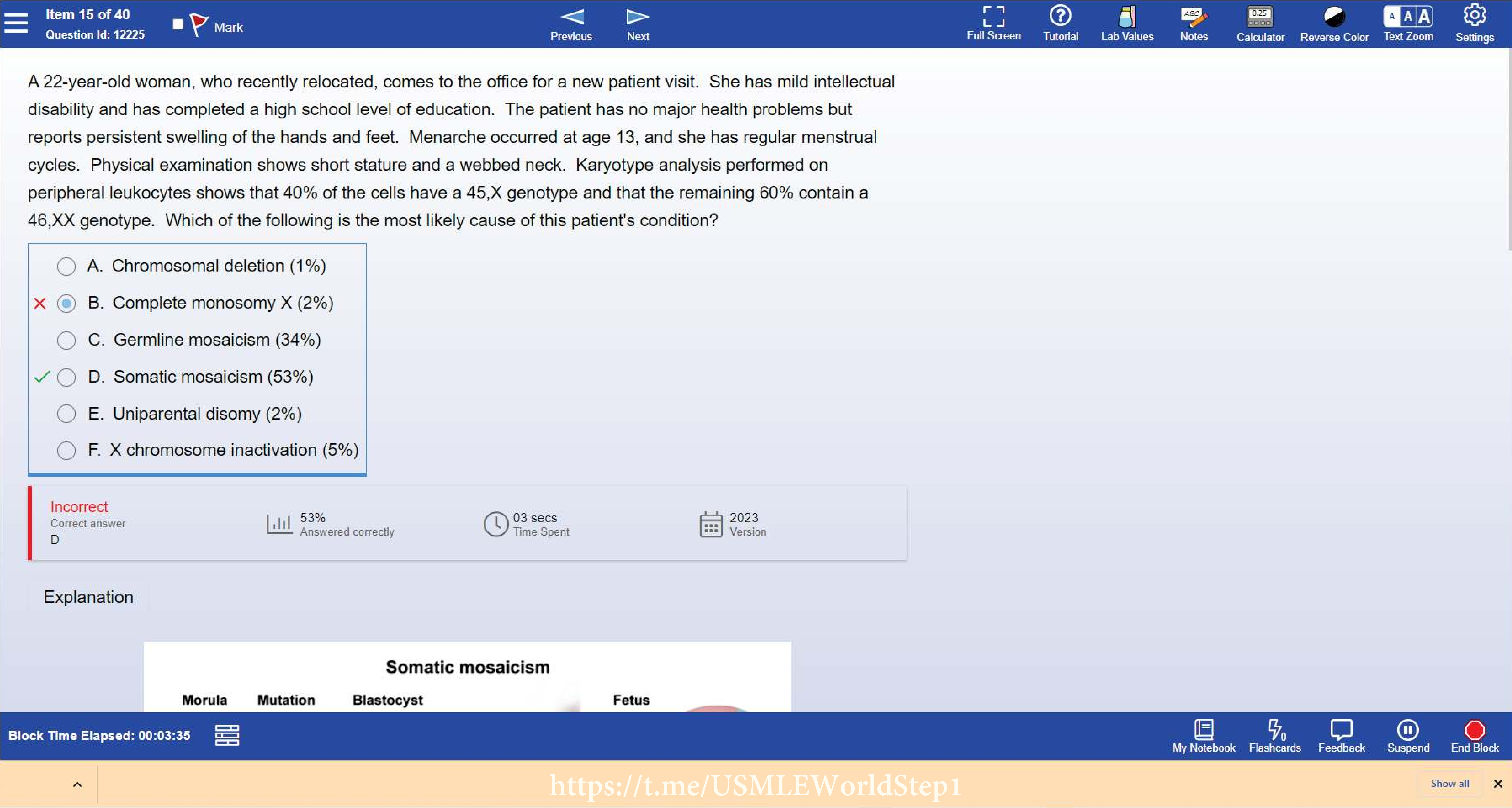
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Question Id: 12225
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A 22-year-old woman, who recently relocated, comes to the office for a new patient visit. She has mild intellectual disability and has completed a high school level of education. The patient has no major health problems but reports persistent swelling of the hands and feet. Menarche occurred at age 13, and she has regular menstrual cycles. Physical examination shows short stature and a webbed neck. Karyotype analysis performed on peripheral leukocytes shows that 40% of the cells have a 45,X genotype and that the remaining 60% contain a 46,XX genotype. Which of the following is the most likely cause of this patient's condition?

○ A. Chromosomal deletion (1%)

✗ ● B. Complete monosomy X (2%)

○ C. Germline mosaicism (34%)

✓ ○ D. Somatic mosaicism (53%)

○ E. Uniparental disomy (2%)

○ F. X chromosome inactivation (5%)

Incorrect
Correct answer
D

53%
Answered correctly

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Explanation

Somatic mosaicism

Morula
Mutation
Blastocyst
Fetus
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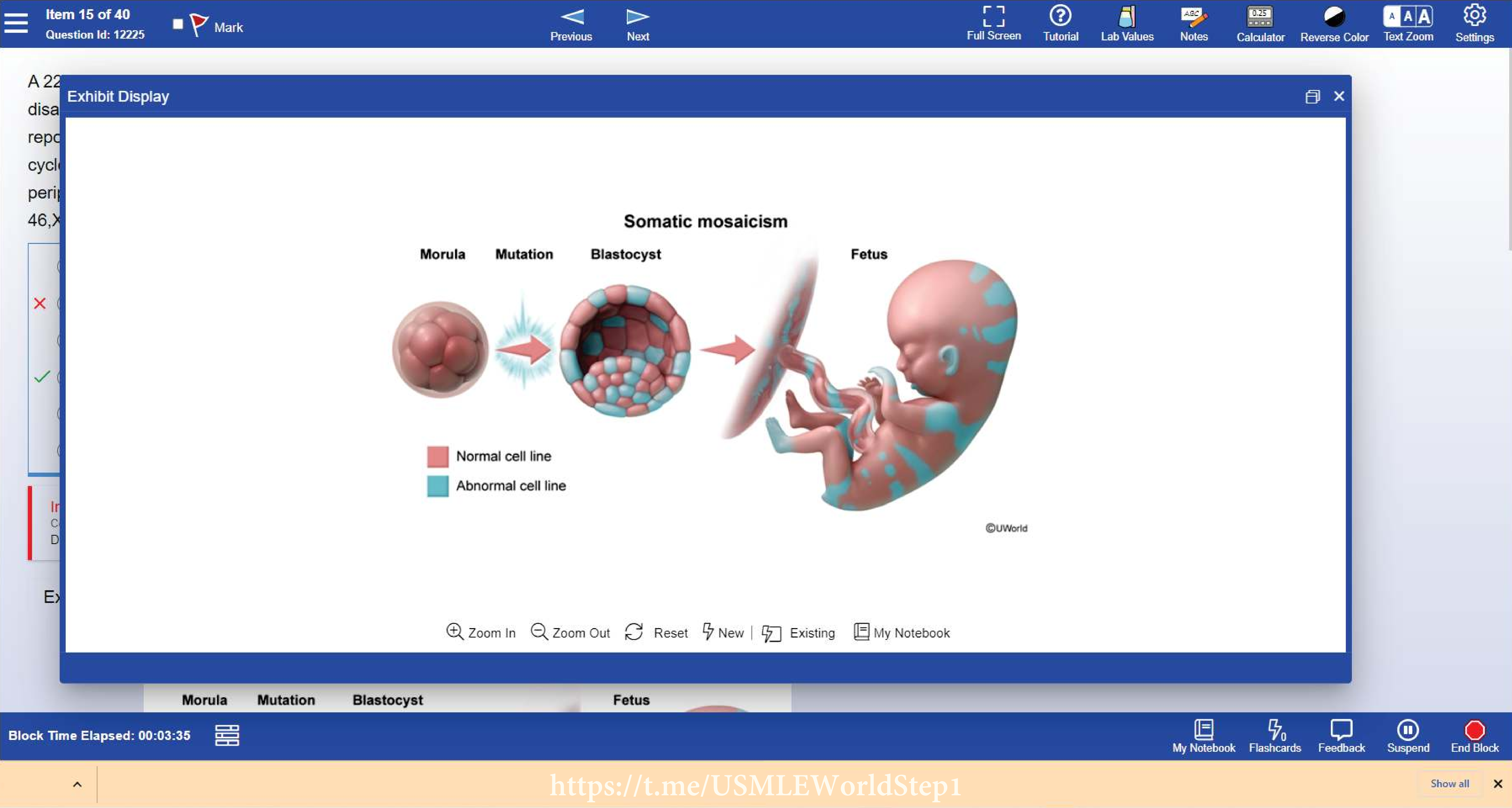

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Question Id: 12225

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Exhibit Display

Somatic mosaicism

Morula
Mutation
Blastocyst
Fetus
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🟦 Abnormal cell line
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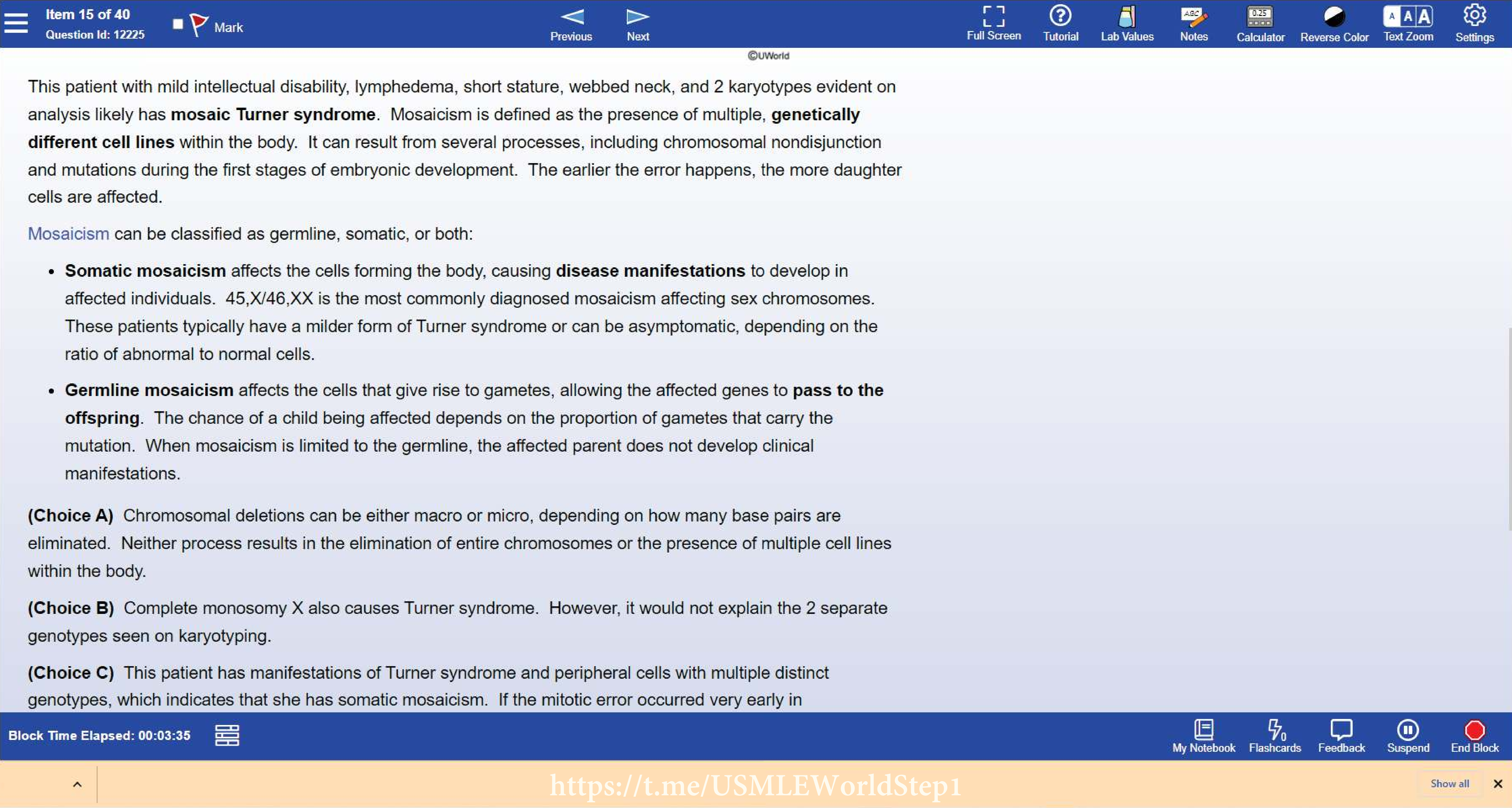
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This patient with mild intellectual disability, lymphedema, short stature, webbed neck, and 2 karyotypes evident on analysis likely has **mosaic Turner syndrome**. Mosaicism is defined as the presence of multiple, **genetically different cell lines** within the body. It can result from several processes, including chromosomal nondisjunction and mutations during the first stages of embryonic development. The earlier the error happens, the more daughter cells are affected.

Mosaicism can be classified as germline, somatic, or both:

- **Somatic mosaicism** affects the cells forming the body, causing **disease manifestations** to develop in affected individuals. 45,X/46,XX is the most commonly diagnosed mosaicism affecting sex chromosomes. These patients typically have a milder form of Turner syndrome or can be asymptomatic, depending on the ratio of abnormal to normal cells.
- **Germline mosaicism** affects the cells that give rise to gametes, allowing the affected genes to **pass to the offspring**. The chance of a child being affected depends on the proportion of gametes that carry the mutation. When mosaicism is limited to the germline, the affected parent does not develop clinical manifestations.

(Choice A) Chromosomal deletions can be either macro or micro, depending on how many base pairs are eliminated. Neither process results in the elimination of entire chromosomes or the presence of multiple cell lines within the body.

(Choice B) Complete monosomy X also causes Turner syndrome. However, it would not explain the 2 separate genotypes seen on karyotyping.

(Choice C) This patient has manifestations of Turner syndrome and peripheral cells with multiple distinct genotypes, which indicates that she has somatic mosaicism. If the mitotic error occurred very early in

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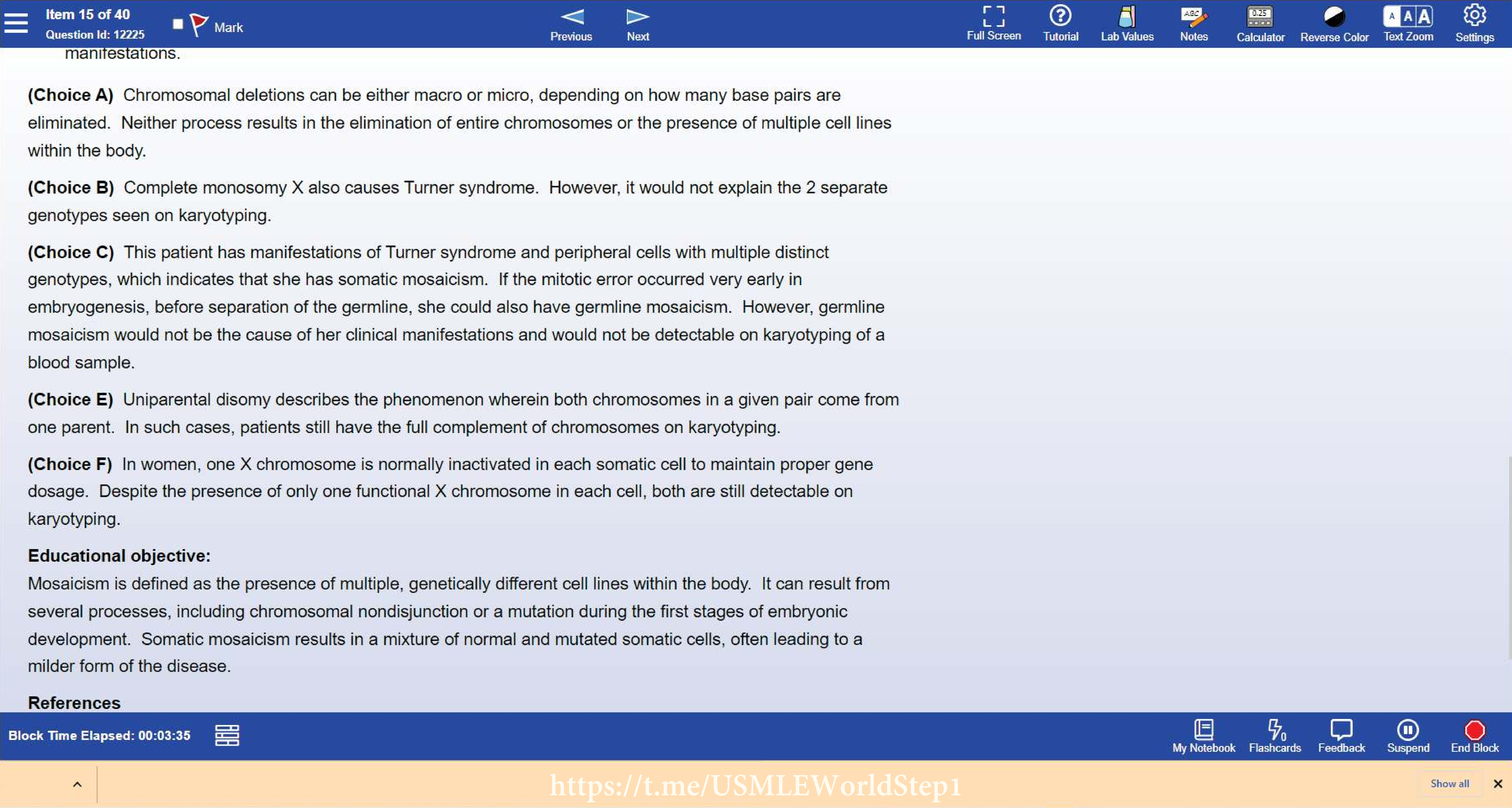
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(Choice B) Complete monosomy X also causes Turner syndrome. However, it would not explain the 2 separate genotypes seen on karyotyping.

(Choice C) This patient has manifestations of Turner syndrome and peripheral cells with multiple distinct genotypes, which indicates that she has somatic mosaicism. If the mitotic error occurred very early in embryogenesis, before separation of the germline, she could also have germline mosaicism. However, germline mosaicism would not be the cause of her clinical manifestations and would not be detectable on karyotyping of a blood sample.

(Choice E) Uniparental disomy describes the phenomenon wherein both chromosomes in a given pair come from one parent. In such cases, patients still have the full complement of chromosomes on karyotyping.

(Choice F) In women, one X chromosome is normally inactivated in each somatic cell to maintain proper gene dosage. Despite the presence of only one functional X chromosome in each cell, both are still detectable on karyotyping.

Educational objective:
Mosaicism is defined as the presence of multiple, genetically different cell lines within the body. It can result from several processes, including chromosomal nondisjunction or a mutation during the first stages of embryonic development. Somatic mosaicism results in a mixture of normal and mutated somatic cells, often leading to a milder form of the disease.

References

🟥 Normal cell line

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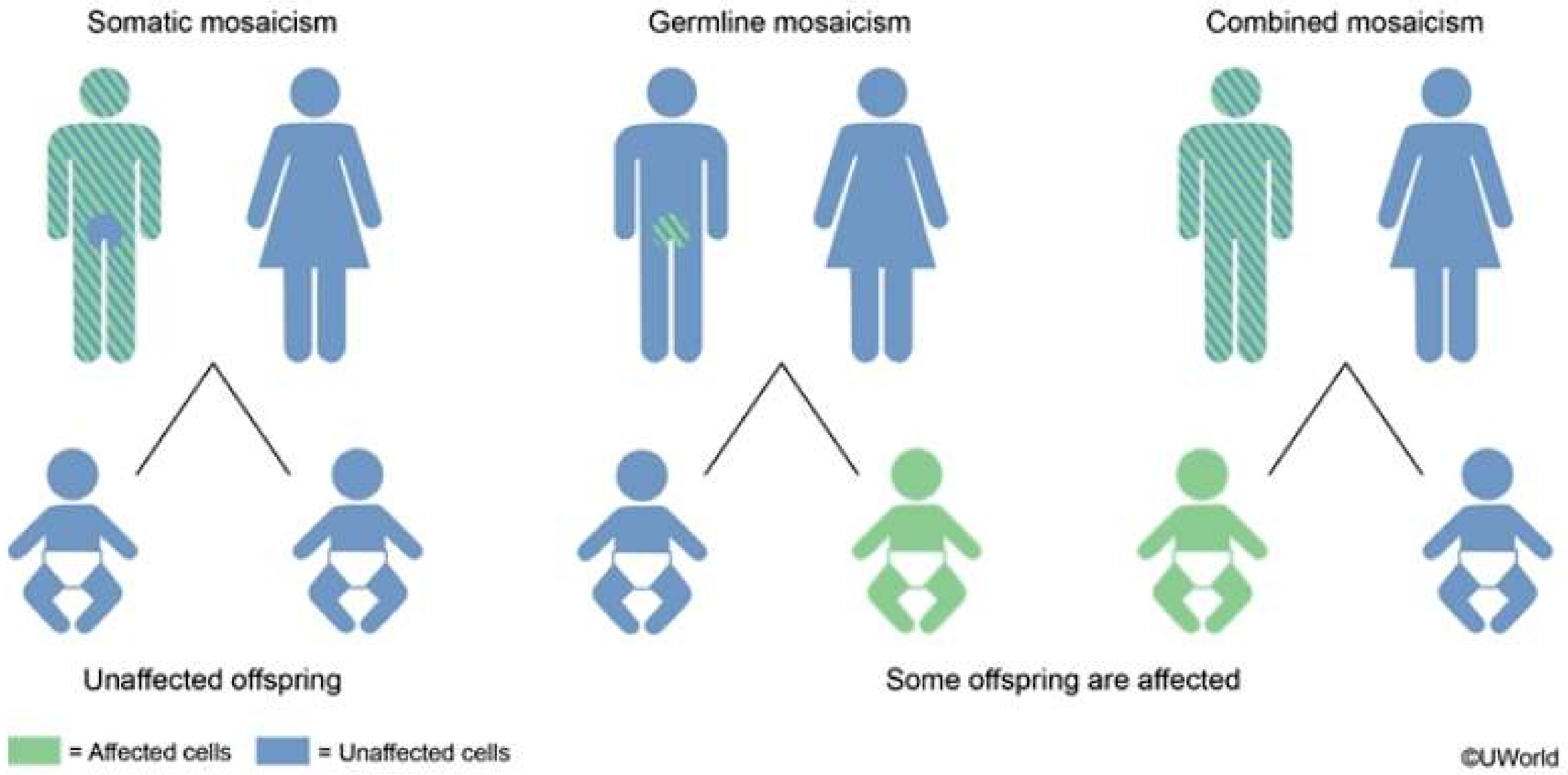
Mosaicism


Somatic mosaicism
Germline mosaicism
Combined mosaicism
Unaffected offspring
Some offspring are affected
🟩 = Affected cells
🟦 = Unaffected cells
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(Choice B) Complete monosomy X also causes Turner syndrome. However, it would not explain the 2 separate

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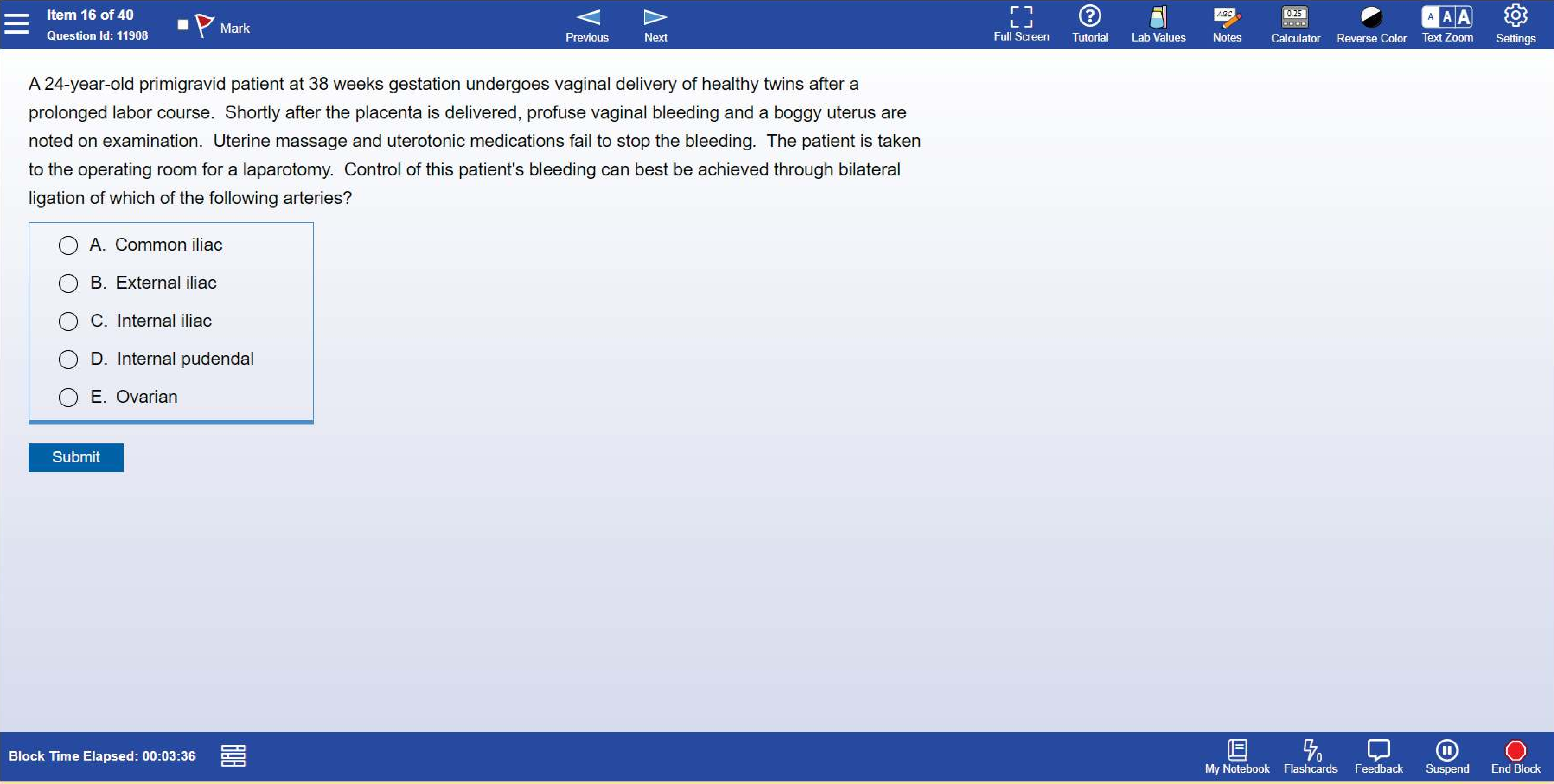
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A 24-year-old primigravid patient at 38 weeks gestation undergoes vaginal delivery of healthy twins after a prolonged labor course. Shortly after the placenta is delivered, profuse vaginal bleeding and a boggy uterus are noted on examination. Uterine massage and uterotonic medications fail to stop the bleeding. The patient is taken to the operating room for a laparotomy. Control of this patient's bleeding can best be achieved through bilateral ligation of which of the following arteries?

○ A. Common iliac
○ B. External iliac
○ C. Internal iliac
○ D. Internal pudendal
○ E. Ovarian

Submit

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- ○ A. Common iliac (2%)
- ✗ ● B. External iliac (5%)
- ✓ ○ C. Internal iliac (71%)
- ○ D. Internal pudendal (11%)
- ○ E. Ovarian (9%)

Incorrect
Correct answer
C

71%
Answered correctly

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Explanation

Branches of the internal iliac artery in the female

Common iliac artery
Internal iliac artery
External
Superior

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Question Id: 11908

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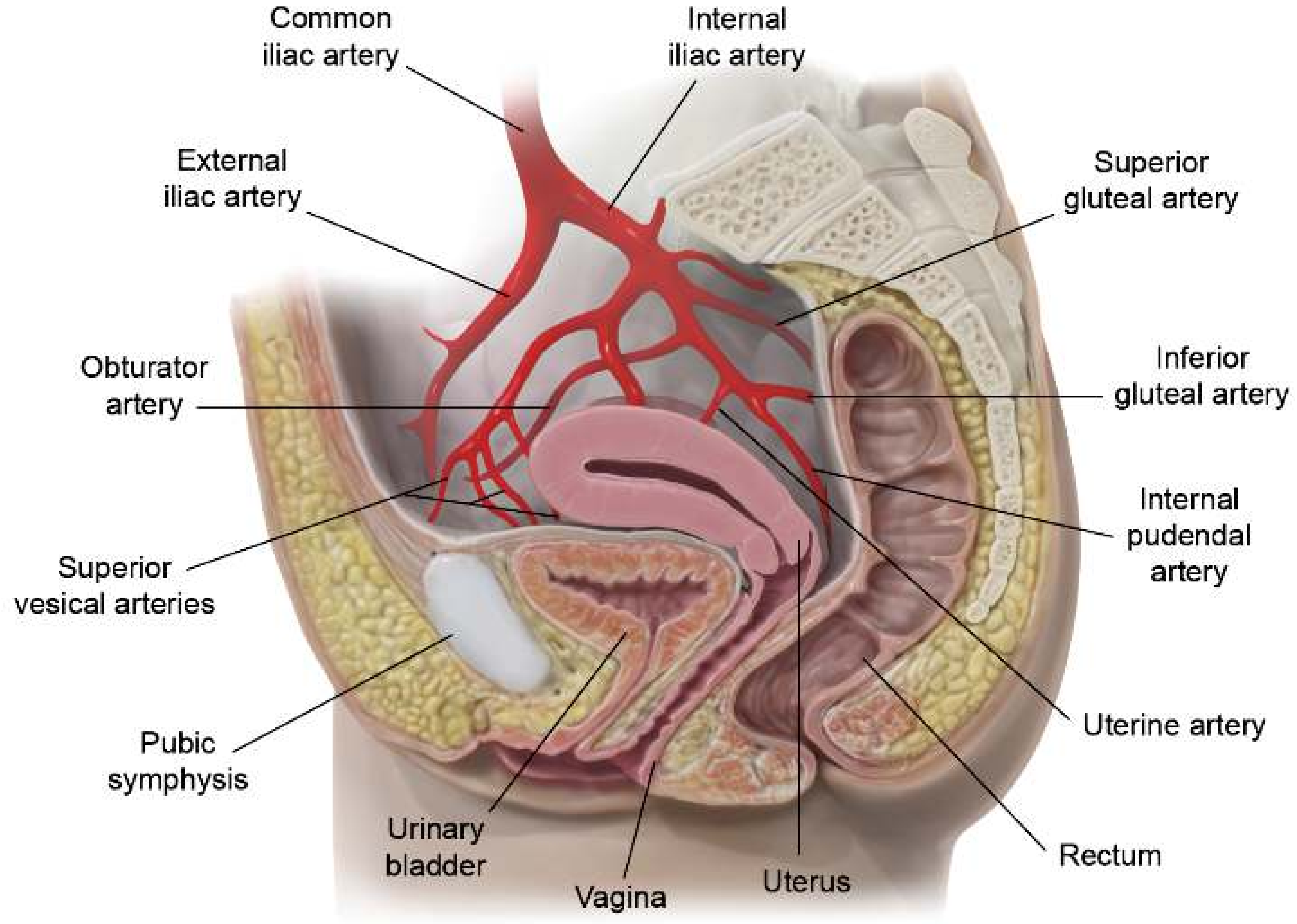
Branches of the internal iliac artery in the female


Common iliac artery
Internal iliac artery
External iliac artery
Superior gluteal artery
Obturator artery
Inferior gluteal artery
Internal pudendal artery
Superior vesical arteries
Pubic symphysis
Uterine artery
Urinary bladder
Vagina
Uterus
Rectum

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External Superior

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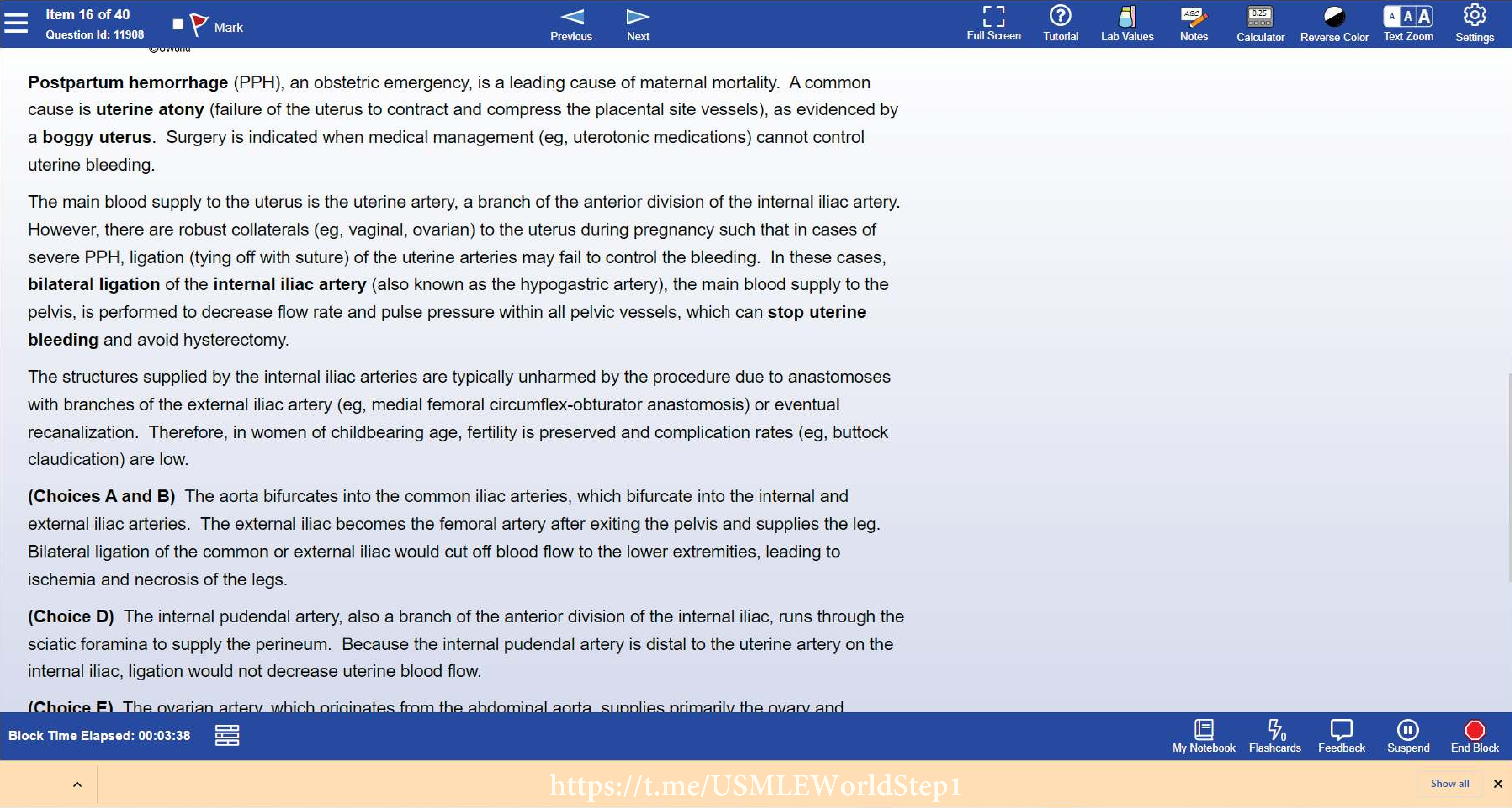


Postpartum hemorrhage (PPH), an obstetric emergency, is a leading cause of maternal mortality. A common cause is **uterine atony** (failure of the uterus to contract and compress the placental site vessels), as evidenced by a **boggy uterus**. Surgery is indicated when medical management (eg, uterotonic medications) cannot control uterine bleeding.

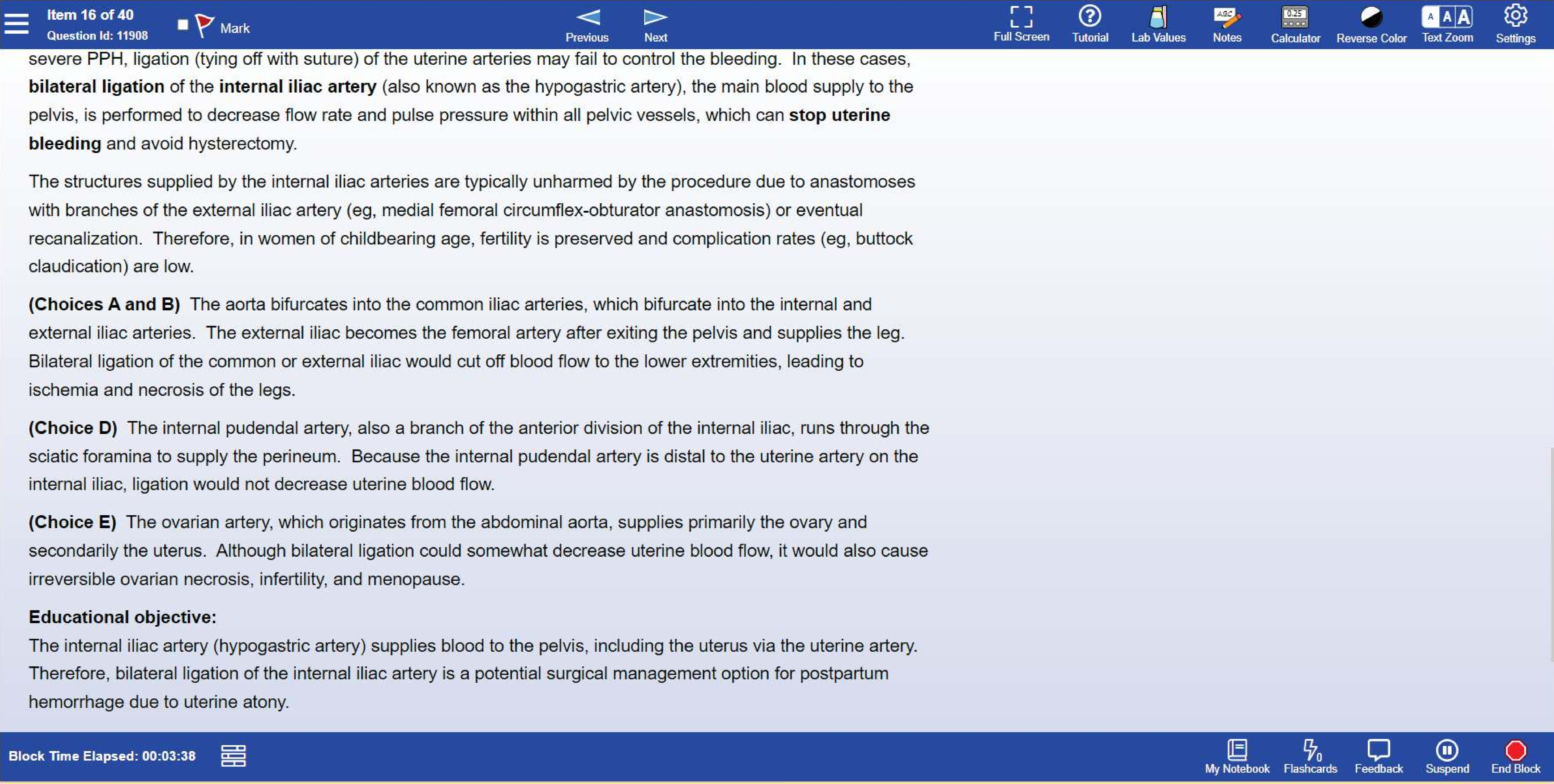
The main blood supply to the uterus is the uterine artery, a branch of the anterior division of the internal iliac artery. However, there are robust collaterals (eg, vaginal, ovarian) to the uterus during pregnancy such that in cases of severe PPH, ligation (tying off with suture) of the uterine arteries may fail to control the bleeding. In these cases, **bilateral ligation** of the **internal iliac artery** (also known as the hypogastric artery), the main blood supply to the pelvis, is performed to decrease flow rate and pulse pressure within all pelvic vessels, which can **stop uterine bleeding** and avoid hysterectomy.

The structures supplied by the internal iliac arteries are typically unharmed by the procedure due to anastomoses with branches of the external iliac artery (eg, medial femoral circumflex-obturator anastomosis) or eventual recanalization. Therefore, in women of childbearing age, fertility is preserved and complication rates (eg, buttock claudication) are low.

(Choices A and B) The aorta bifurcates into the common iliac arteries, which bifurcate into the internal and external iliac arteries. The external iliac becomes the femoral artery after exiting the pelvis and supplies the leg. Bilateral ligation of the common or external iliac would cut off blood flow to the lower extremities, leading to ischemia and necrosis of the legs.

(Choice D) The internal pudendal artery, also a branch of the anterior division of the internal iliac, runs through the sciatic foramina to supply the perineum. Because the internal pudendal artery is distal to the uterine artery on the internal iliac, ligation would not decrease uterine blood flow.

(Choice E) The ovarian artery, which originates from the abdominal aorta, supplies primarily the ovary and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(Choice E) The ovarian artery, which originates from the abdominal aorta, supplies primarily the ovary and secondarily the uterus. Although bilateral ligation could somewhat decrease uterine blood flow, it would also cause irreversible ovarian necrosis, infertility, and menopause.

Educational objective:

The internal iliac artery (hypogastric artery) supplies blood to the pelvis, including the uterus via the uterine artery. Therefore, bilateral ligation of the internal iliac artery is a potential surgical management option for postpartum hemorrhage due to uterine atony.

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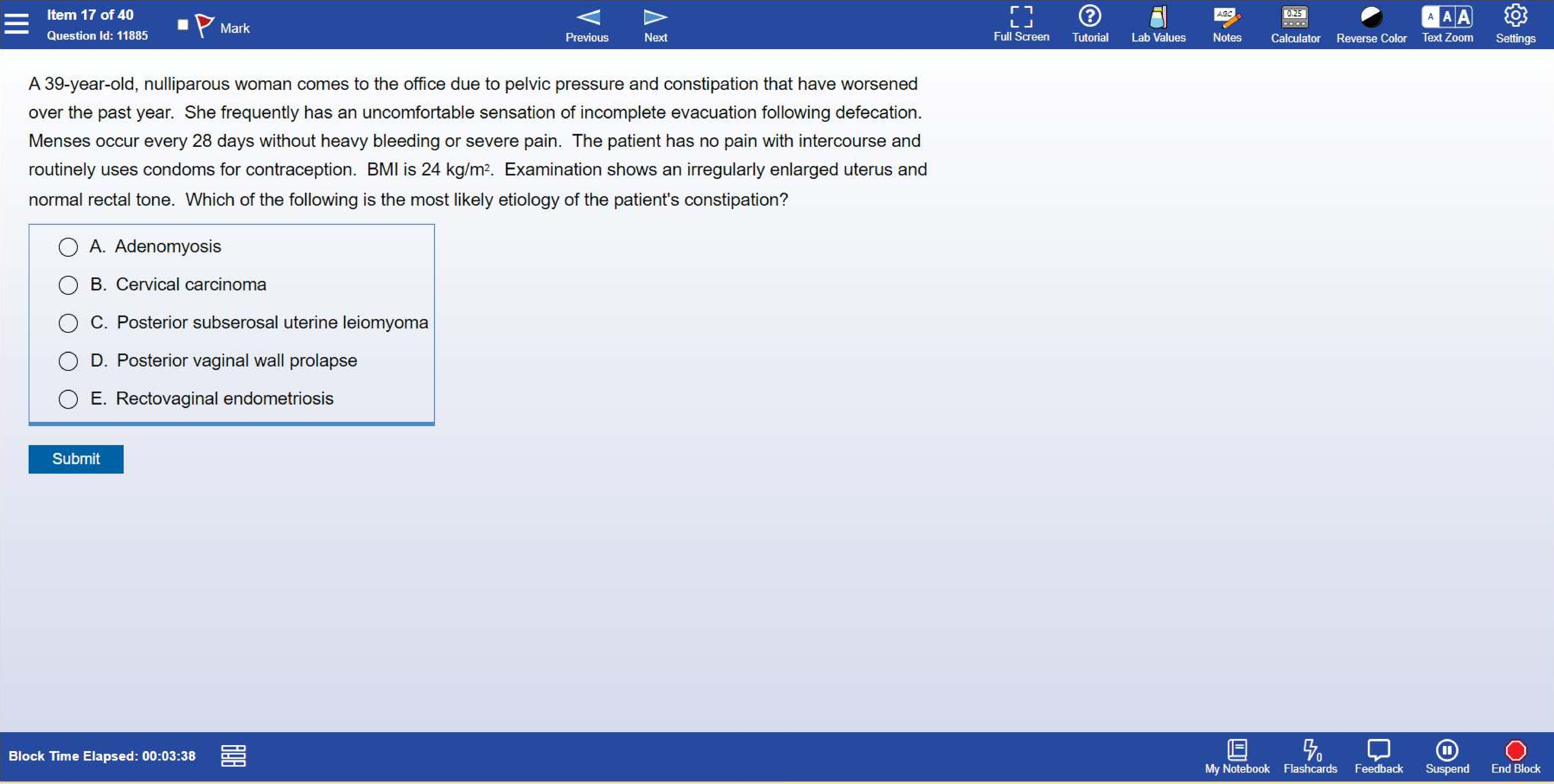
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A 39-year-old, nulliparous woman comes to the office due to pelvic pressure and constipation that have worsened over the past year. She frequently has an uncomfortable sensation of incomplete evacuation following defecation. Menses occur every 28 days without heavy bleeding or severe pain. The patient has no pain with intercourse and routinely uses condoms for contraception. BMI is 24 kg/m^2. Examination shows an irregularly enlarged uterus and normal rectal tone. Which of the following is the most likely etiology of the patient's constipation?

- ○ A. Adenomyosis
- ○ B. Cervical carcinoma
- ○ C. Posterior subserosal uterine leiomyoma
- ○ D. Posterior vaginal wall prolapse
- ○ E. Rectovaginal endometriosis

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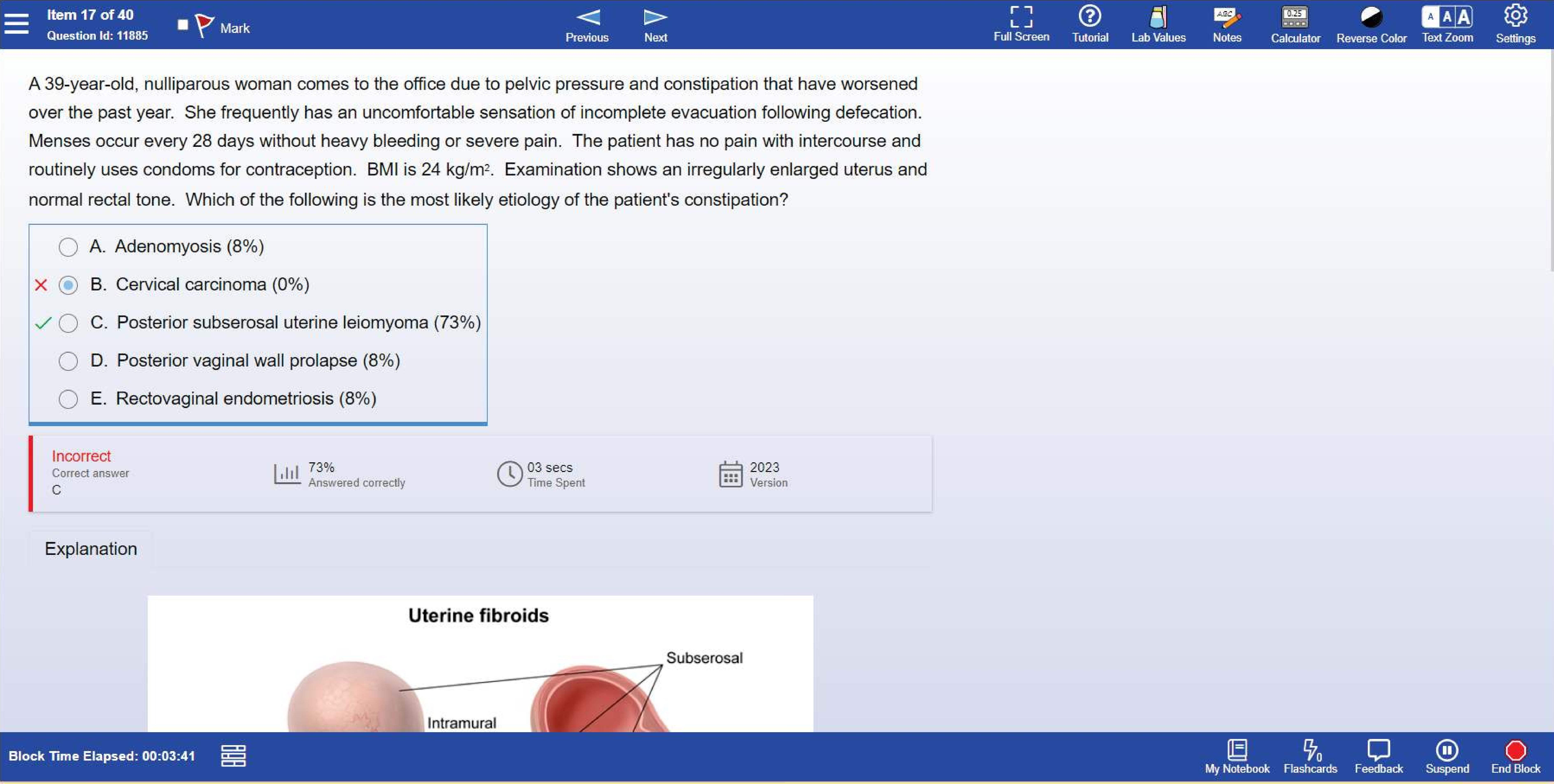
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○ A. Adenomyosis (8%)

✗ ● B. Cervical carcinoma (0%)

✓ ○ C. Posterior subserosal uterine leiomyoma (73%)

○ D. Posterior vaginal wall prolapse (8%)

○ E. Rectovaginal endometriosis (8%)

Incorrect
Correct answer
C

73%
Answered correctly

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Explanation

Uterine fibroids

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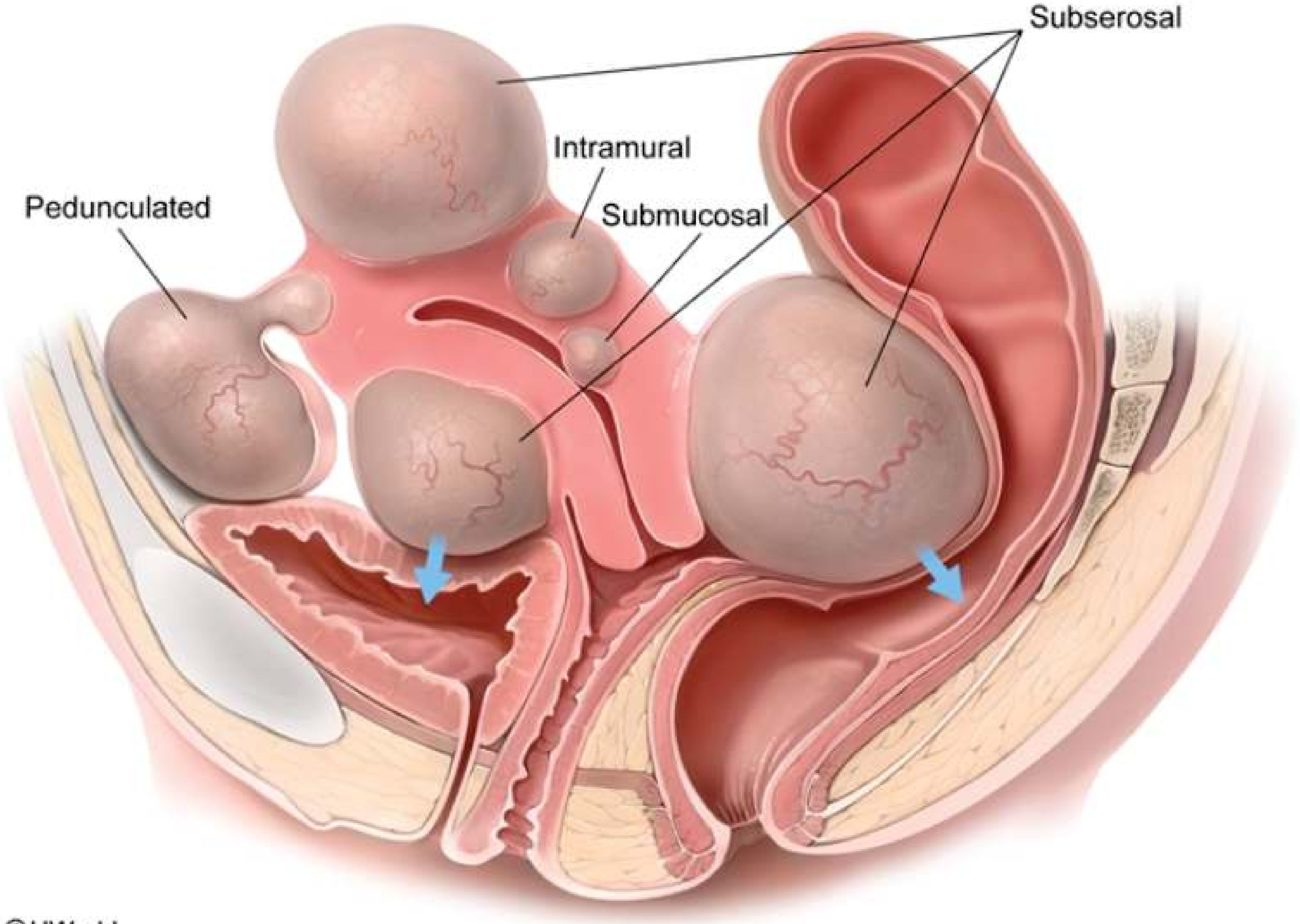
Uterine fibroids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Submucosal

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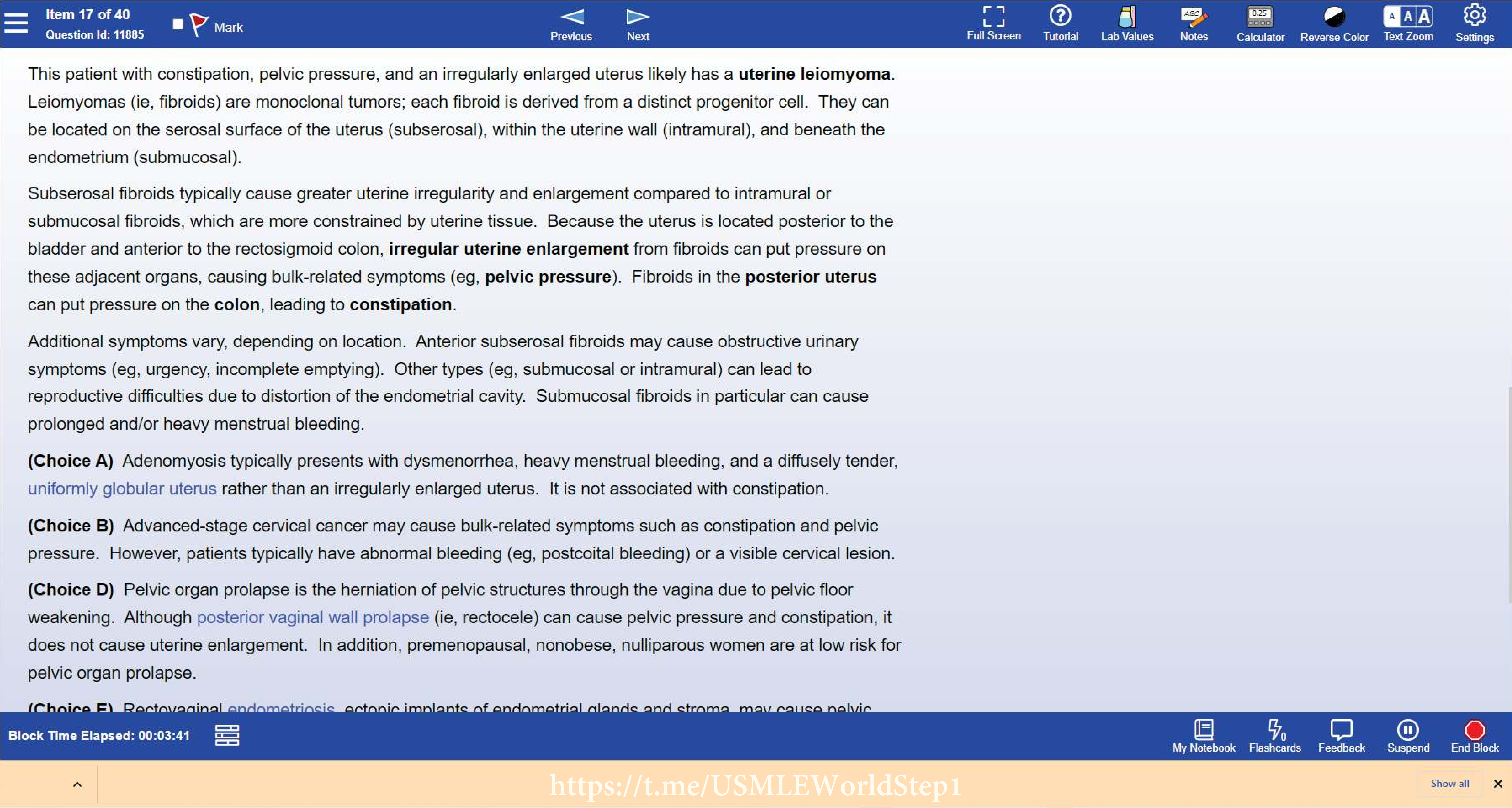


This patient with constipation, pelvic pressure, and an irregularly enlarged uterus likely has a **uterine leiomyoma**. Leiomyomas (ie, fibroids) are monoclonal tumors; each fibroid is derived from a distinct progenitor cell. They can be located on the serosal surface of the uterus (subserosal), within the uterine wall (intramural), and beneath the endometrium (submucosal).

Subserosal fibroids typically cause greater uterine irregularity and enlargement compared to intramural or submucosal fibroids, which are more constrained by uterine tissue. Because the uterus is located posterior to the bladder and anterior to the rectosigmoid colon, **irregular uterine enlargement** from fibroids can put pressure on these adjacent organs, causing bulk-related symptoms (eg, **pelvic pressure**). Fibroids in the **posterior uterus** can put pressure on the **colon**, leading to **constipation**.

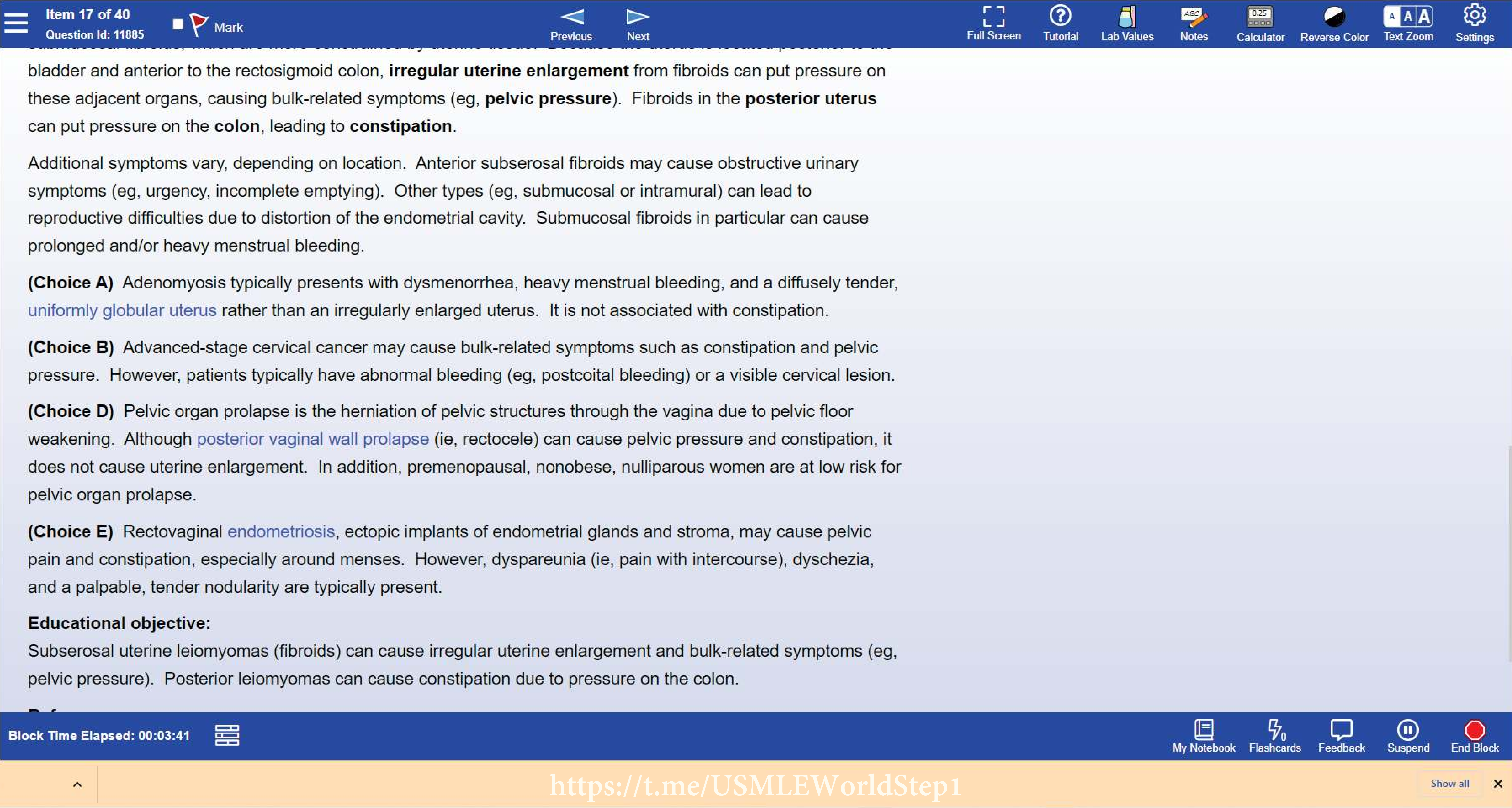
Additional symptoms vary, depending on location. Anterior subserosal fibroids may cause obstructive urinary symptoms (eg, urgency, incomplete emptying). Other types (eg, submucosal or intramural) can lead to reproductive difficulties due to distortion of the endometrial cavity. Submucosal fibroids in particular can cause prolonged and/or heavy menstrual bleeding.

(Choice A) Adenomyosis typically presents with dysmenorrhea, heavy menstrual bleeding, and a diffusely tender, uniformly globular uterus rather than an irregularly enlarged uterus. It is not associated with constipation.

(Choice B) Advanced-stage cervical cancer may cause bulk-related symptoms such as constipation and pelvic pressure. However, patients typically have abnormal bleeding (eg, postcoital bleeding) or a visible cervical lesion.

(Choice D) Pelvic organ prolapse is the herniation of pelvic structures through the vagina due to pelvic floor weakening. Although posterior vaginal wall prolapse (ie, rectocele) can cause pelvic pressure and constipation, it does not cause uterine enlargement. In addition, premenopausal, nonobese, nulliparous women are at low risk for pelvic organ prolapse.

(Choice E) Rectovaginal endometriosis, ectopic implants of endometrial glands and stroma, may cause pelvic



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bladder and anterior to the rectosigmoid colon, **irregular uterine enlargement** from fibroids can put pressure on these adjacent organs, causing bulk-related symptoms (eg, **pelvic pressure**). Fibroids in the **posterior uterus** can put pressure on the **colon**, leading to **constipation**.

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(Choice E) Rectovaginal endometriosis, ectopic implants of endometrial glands and stroma, may cause pelvic pain and constipation, especially around menses. However, dyspareunia (ie, pain with intercourse), dyschezia, and a palpable, tender nodularity are typically present.

Educational objective:

Subserosal uterine leiomyomas (fibroids) can cause irregular uterine enlargement and bulk-related symptoms (eg, pelvic pressure). Posterior leiomyomas can cause constipation due to pressure on the colon.

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Educational objective:

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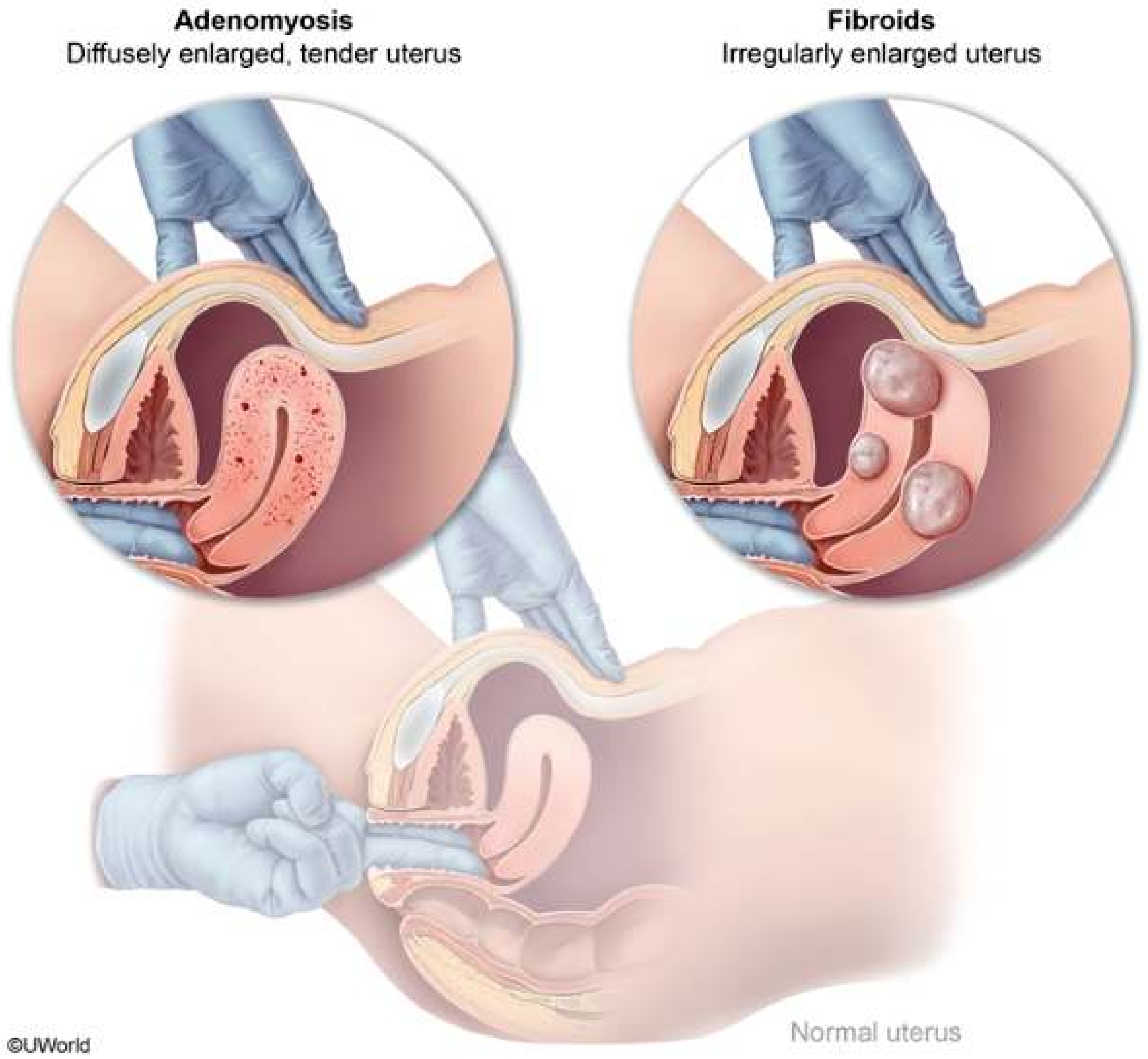
Adenomyosis vs fibroids


Adenomyosis
Diffusely enlarged, tender uterus
Fibroids
Irregularly enlarged uterus
Normal uterus
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endometrium (submucosal).

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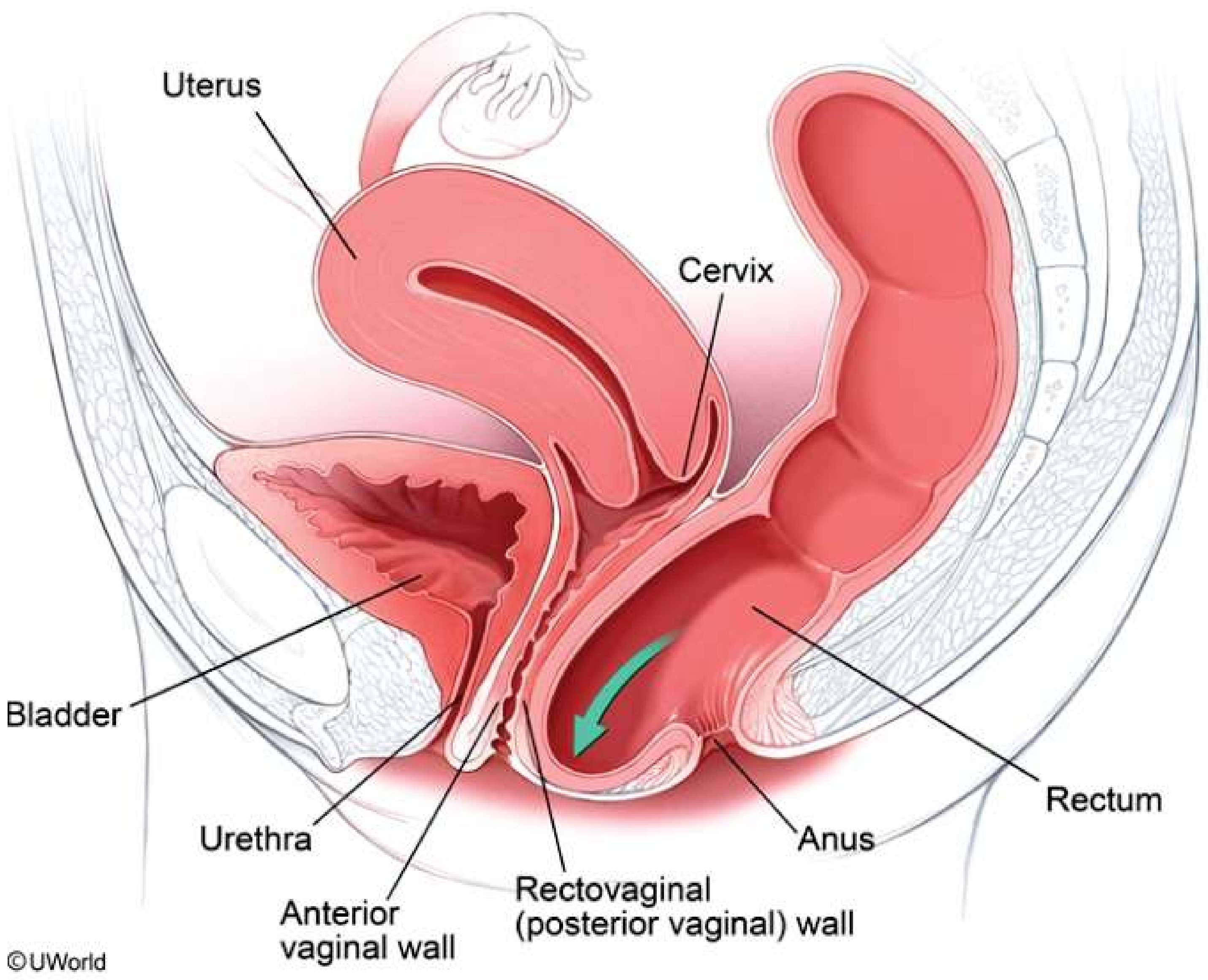
Rectocele, prolapse of posterior vaginal wall


Uterus
Cervix
Bladder
Rectum
Urethra
Anus
Anterior vaginal wall
Rectovaginal (posterior vaginal) wall
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Educational objective:

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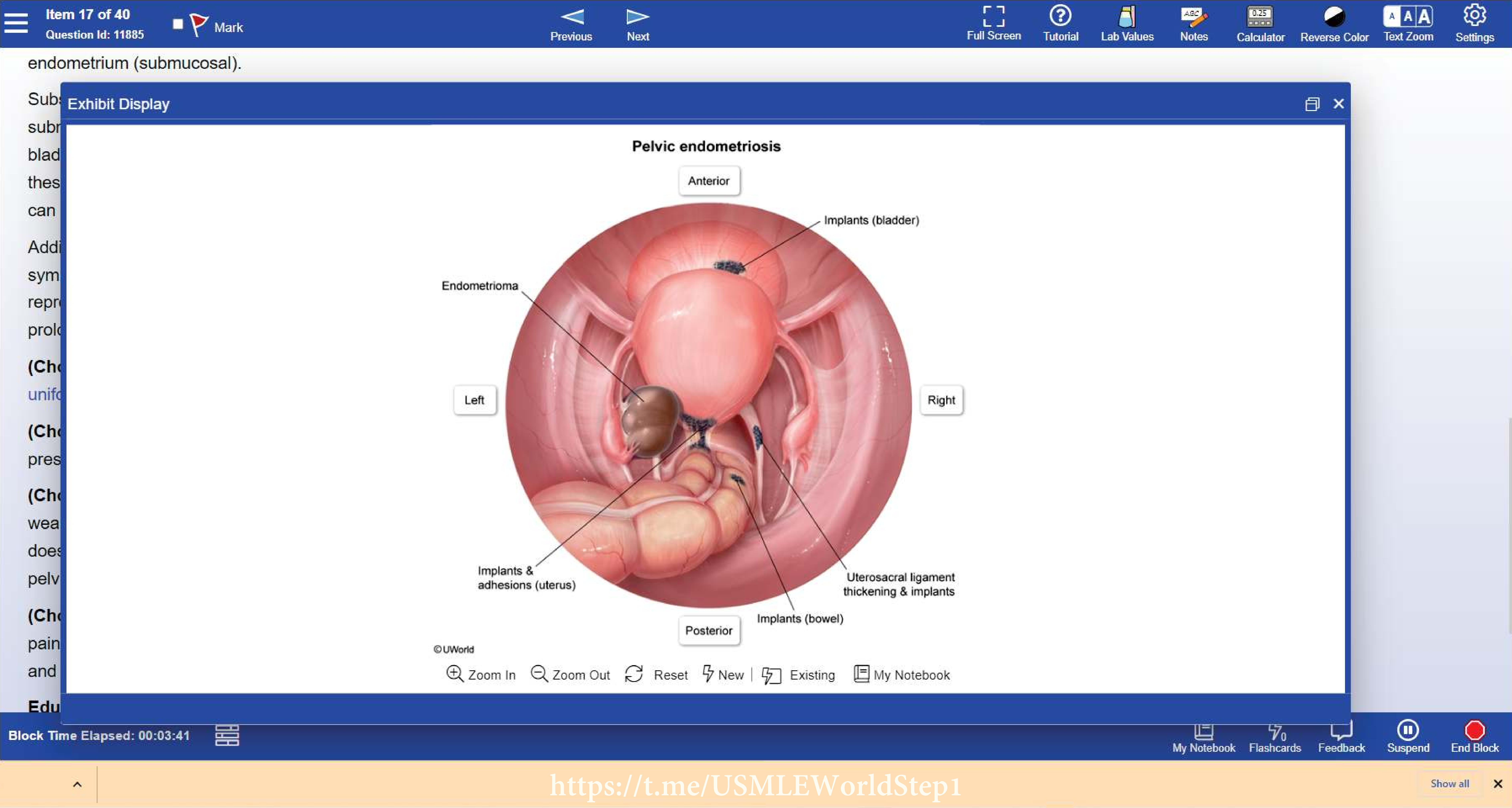
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Anterior
Implants (bladder)
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adhesions (uterus)
Uterosacral ligament
thickening & implants
Implants (bowel)
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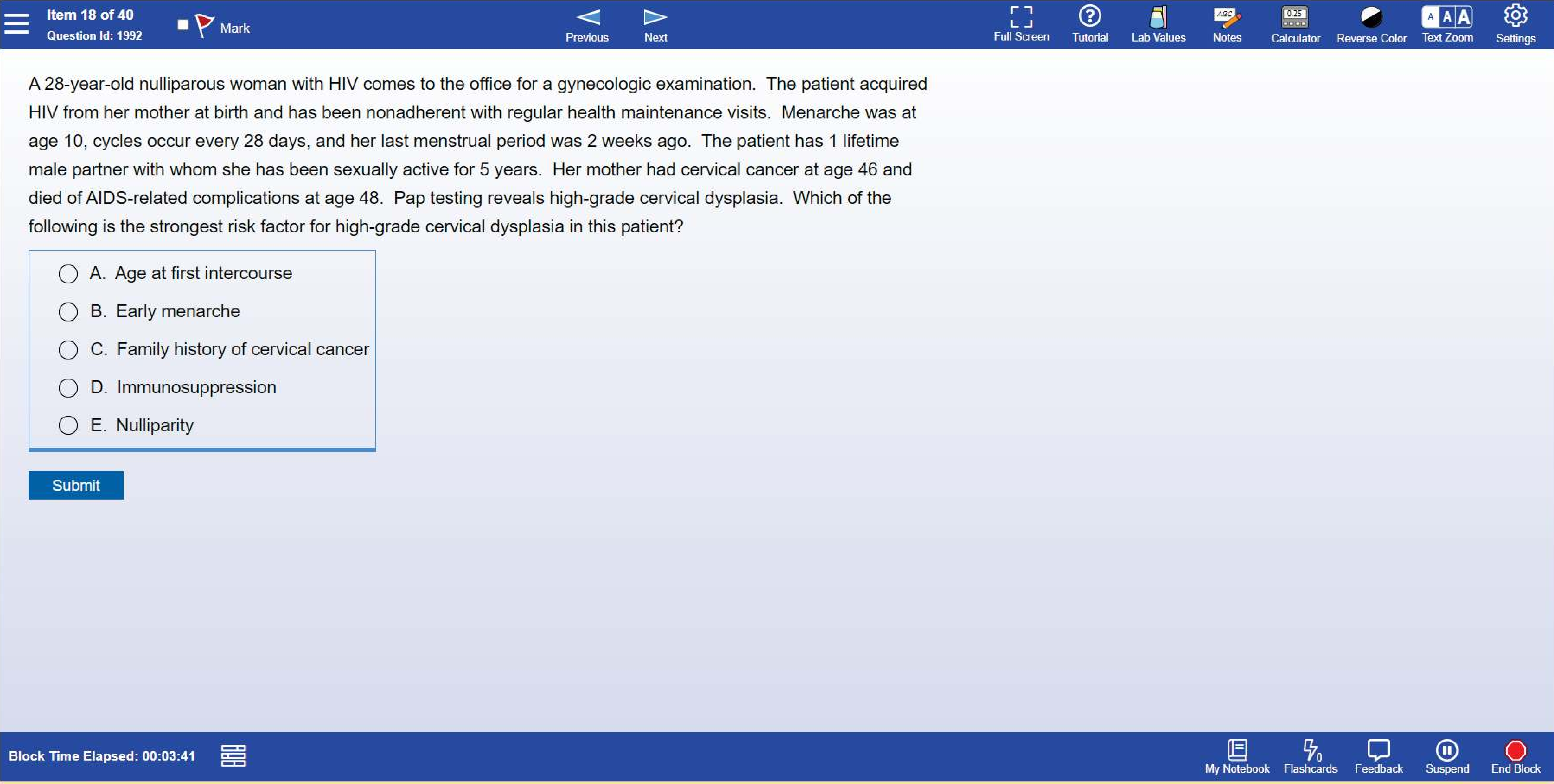
Pelvic endometriosis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A 28-year-old nulliparous woman with HIV comes to the office for a gynecologic examination. The patient acquired HIV from her mother at birth and has been nonadherent with regular health maintenance visits. Menarche was at age 10, cycles occur every 28 days, and her last menstrual period was 2 weeks ago. The patient has 1 lifetime male partner with whom she has been sexually active for 5 years. Her mother had cervical cancer at age 46 and died of AIDS-related complications at age 48. Pap testing reveals high-grade cervical dysplasia. Which of the following is the strongest risk factor for high-grade cervical dysplasia in this patient?

○ A. Age at first intercourse
○ B. Early menarche
○ C. Family history of cervical cancer
○ D. Immunosuppression
○ E. Nulliparity

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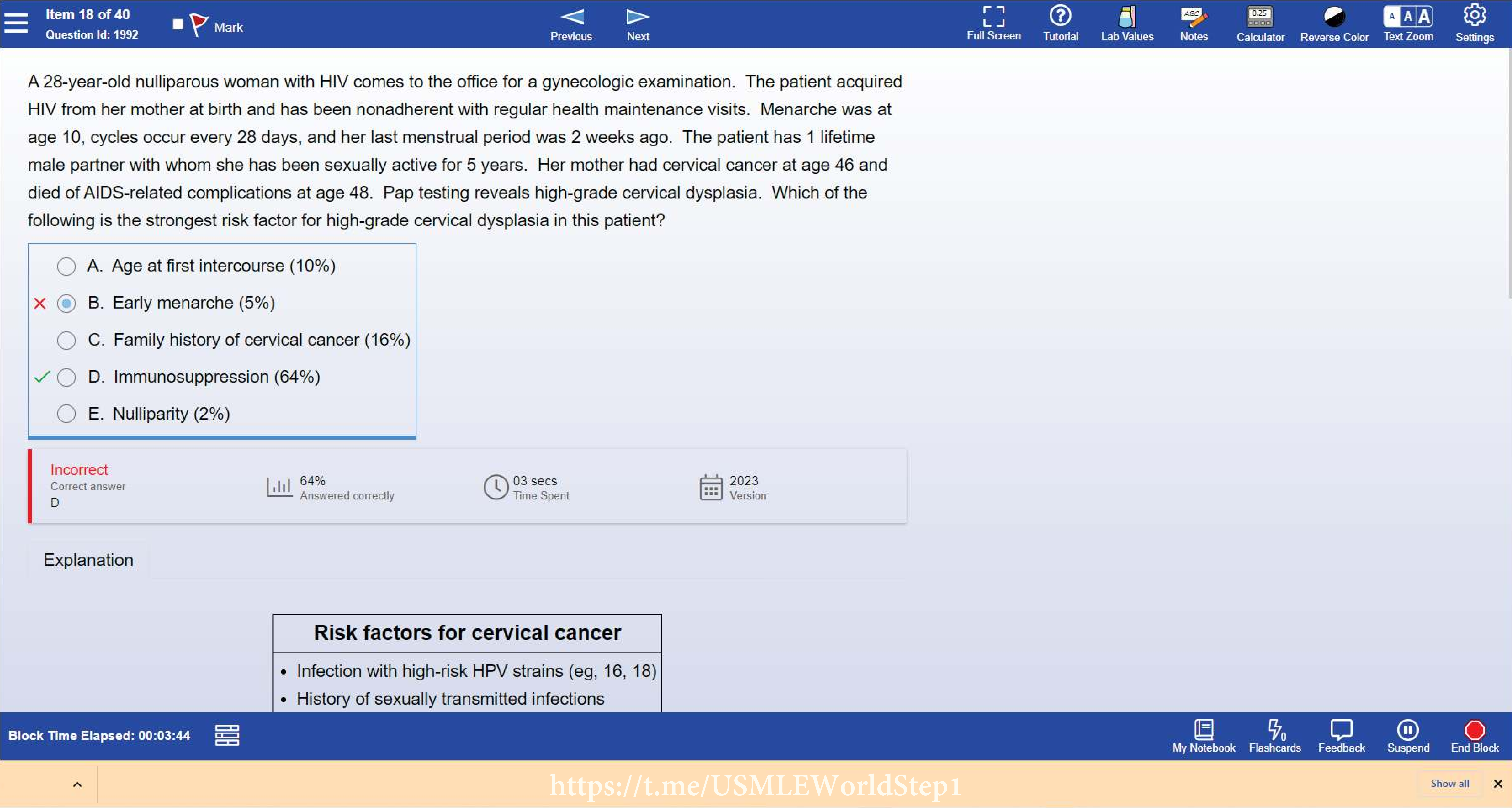
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○ A. Age at first intercourse (10%)
✗ ● B. Early menarche (5%)
○ C. Family history of cervical cancer (16%)
✓ ○ D. Immunosuppression (64%)
○ E. Nulliparity (2%)

Incorrect
Correct answer
D

64%
Answered correctly

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Explanation

Risk factors for cervical cancer
- Infection with high-risk HPV strains (eg, 16, 18) - History of sexually transmitted infections

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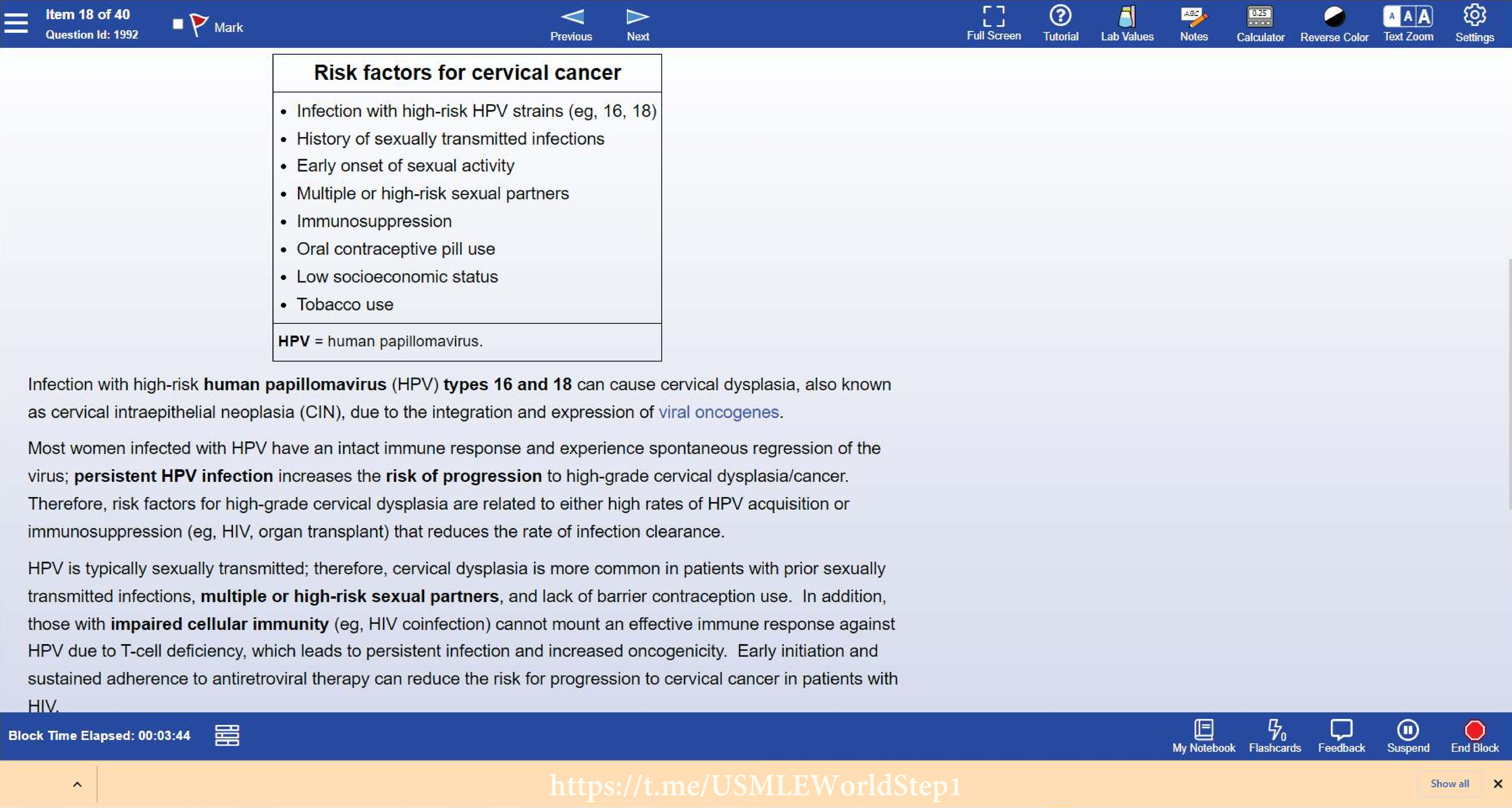
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Risk factors for cervical cancer

- Infection with high-risk HPV strains (eg, 16, 18)
- History of sexually transmitted infections
- Early onset of sexual activity
- Multiple or high-risk sexual partners
- Immunosuppression
- Oral contraceptive pill use
- Low socioeconomic status
- Tobacco use

HPV = human papillomavirus.

Infection with high-risk **human papillomavirus** (HPV) **types 16 and 18** can cause cervical dysplasia, also known as cervical intraepithelial neoplasia (CIN), due to the integration and expression of viral oncogenes.

Most women infected with HPV have an intact immune response and experience spontaneous regression of the virus; **persistent HPV infection** increases the **risk of progression** to high-grade cervical dysplasia/cancer. Therefore, risk factors for high-grade cervical dysplasia are related to either high rates of HPV acquisition or immunosuppression (eg, HIV, organ transplant) that reduces the rate of infection clearance.

HPV is typically sexually transmitted; therefore, cervical dysplasia is more common in patients with prior sexually transmitted infections, **multiple or high-risk sexual partners**, and lack of barrier contraception use. In addition, those with **impaired cellular immunity** (eg, HIV coinfection) cannot mount an effective immune response against HPV due to T-cell deficiency, which leads to persistent infection and increased oncogenicity. Early initiation and sustained adherence to antiretroviral therapy can reduce the risk for progression to cervical cancer in patients with HIV.

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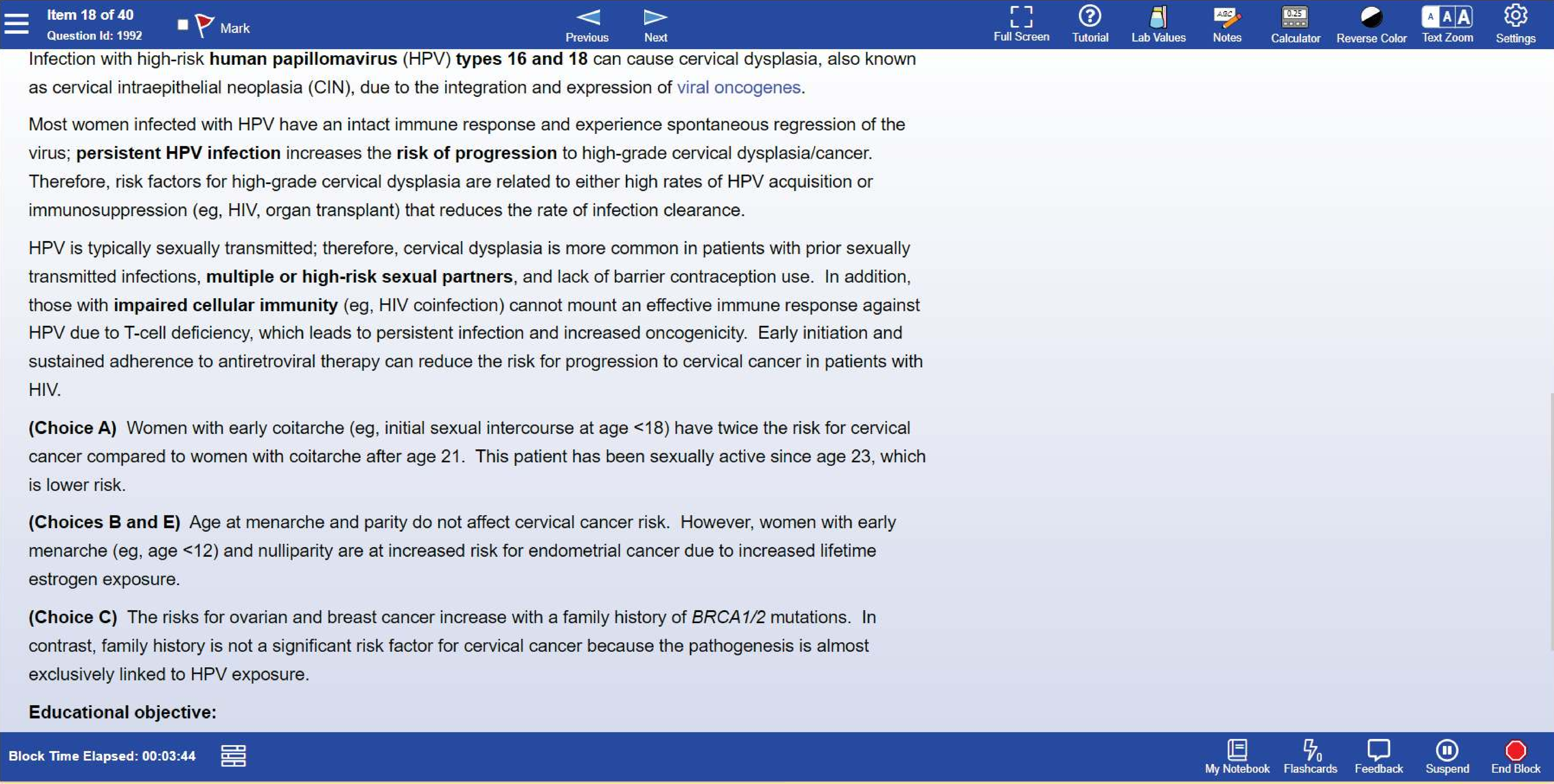

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(Choice A) Women with early coitarche (eg, initial sexual intercourse at age <18) have twice the risk for cervical cancer compared to women with coitarche after age 21. This patient has been sexually active since age 23, which is lower risk.

(Choices B and E) Age at menarche and parity do not affect cervical cancer risk. However, women with early menarche (eg, age <12) and nulliparity are at increased risk for endometrial cancer due to increased lifetime estrogen exposure.

(Choice C) The risks for ovarian and breast cancer increase with a family history of *BRCA1/2* mutations. In contrast, family history is not a significant risk factor for cervical cancer because the pathogenesis is almost exclusively linked to HPV exposure.

Educational objective:

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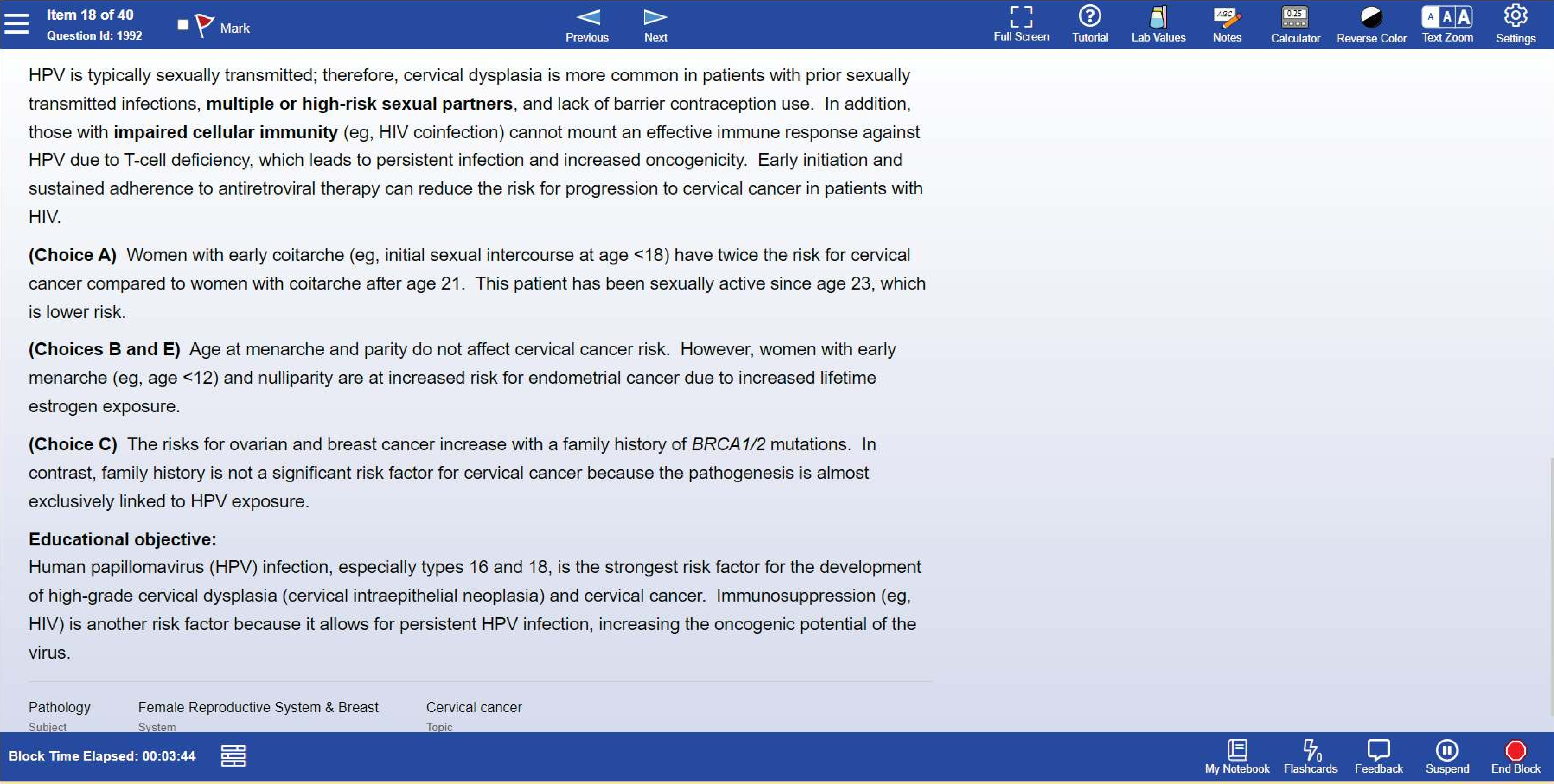
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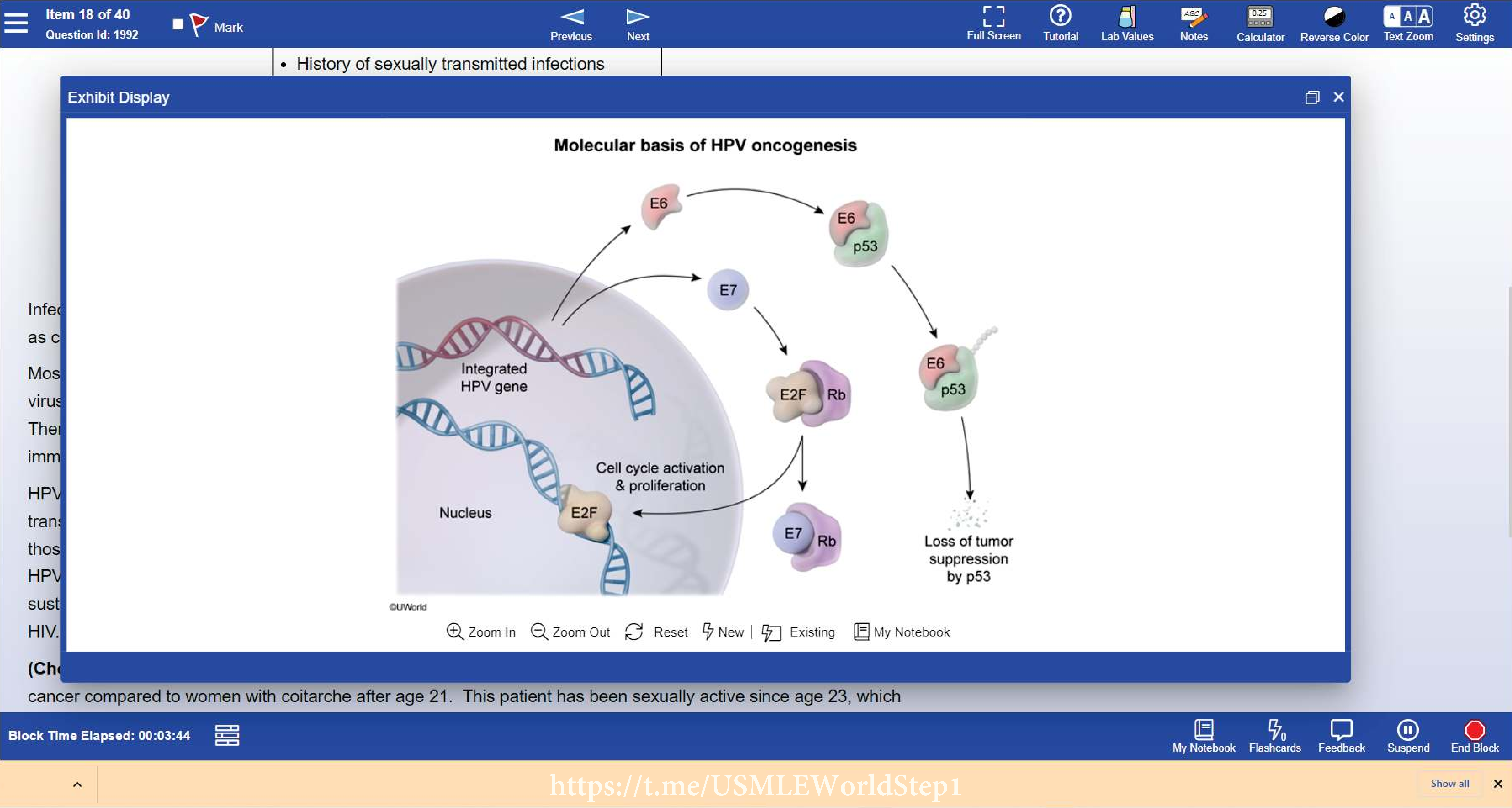
Educational objective:
Human papillomavirus (HPV) infection, especially types 16 and 18, is the strongest risk factor for the development of high-grade cervical dysplasia (cervical intraepithelial neoplasia) and cervical cancer. Immunosuppression (eg, HIV) is another risk factor because it allows for persistent HPV infection, increasing the oncogenic potential of the virus.

Pathology	Female Reproductive System & Breast	Cervical cancer
Subject	System	Topic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- History of sexually transmitted infections

Exhibit Display

Molecular basis of HPV oncogenesis

E6
E6
p53
E7
Integrated
HPV gene
E2F
Rb
E6
p53
Cell cycle activation
& proliferation
Nucleus
E2F
E7
Rb
Loss of tumor
suppression
by p53

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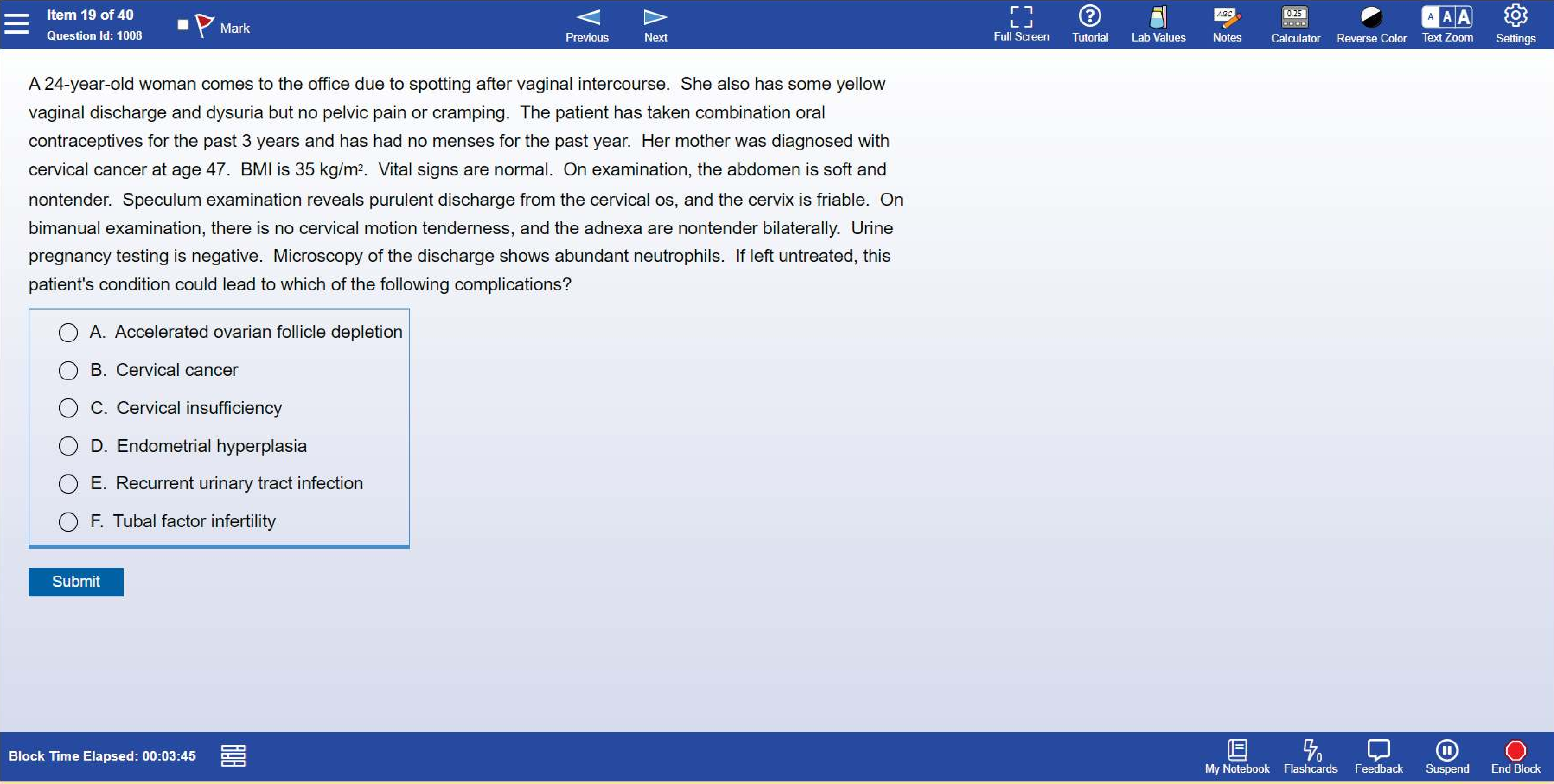
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A 24-year-old woman comes to the office due to spotting after vaginal intercourse. She also has some yellow vaginal discharge and dysuria but no pelvic pain or cramping. The patient has taken combination oral contraceptives for the past 3 years and has had no menses for the past year. Her mother was diagnosed with cervical cancer at age 47. BMI is 35 kg/m^2. Vital signs are normal. On examination, the abdomen is soft and nontender. Speculum examination reveals purulent discharge from the cervical os, and the cervix is friable. On bimanual examination, there is no cervical motion tenderness, and the adnexa are nontender bilaterally. Urine pregnancy testing is negative. Microscopy of the discharge shows abundant neutrophils. If left untreated, this patient's condition could lead to which of the following complications?

○ A. Accelerated ovarian follicle depletion
○ B. Cervical cancer
○ C. Cervical insufficiency
○ D. Endometrial hyperplasia
○ E. Recurrent urinary tract infection
○ F. Tubal factor infertility

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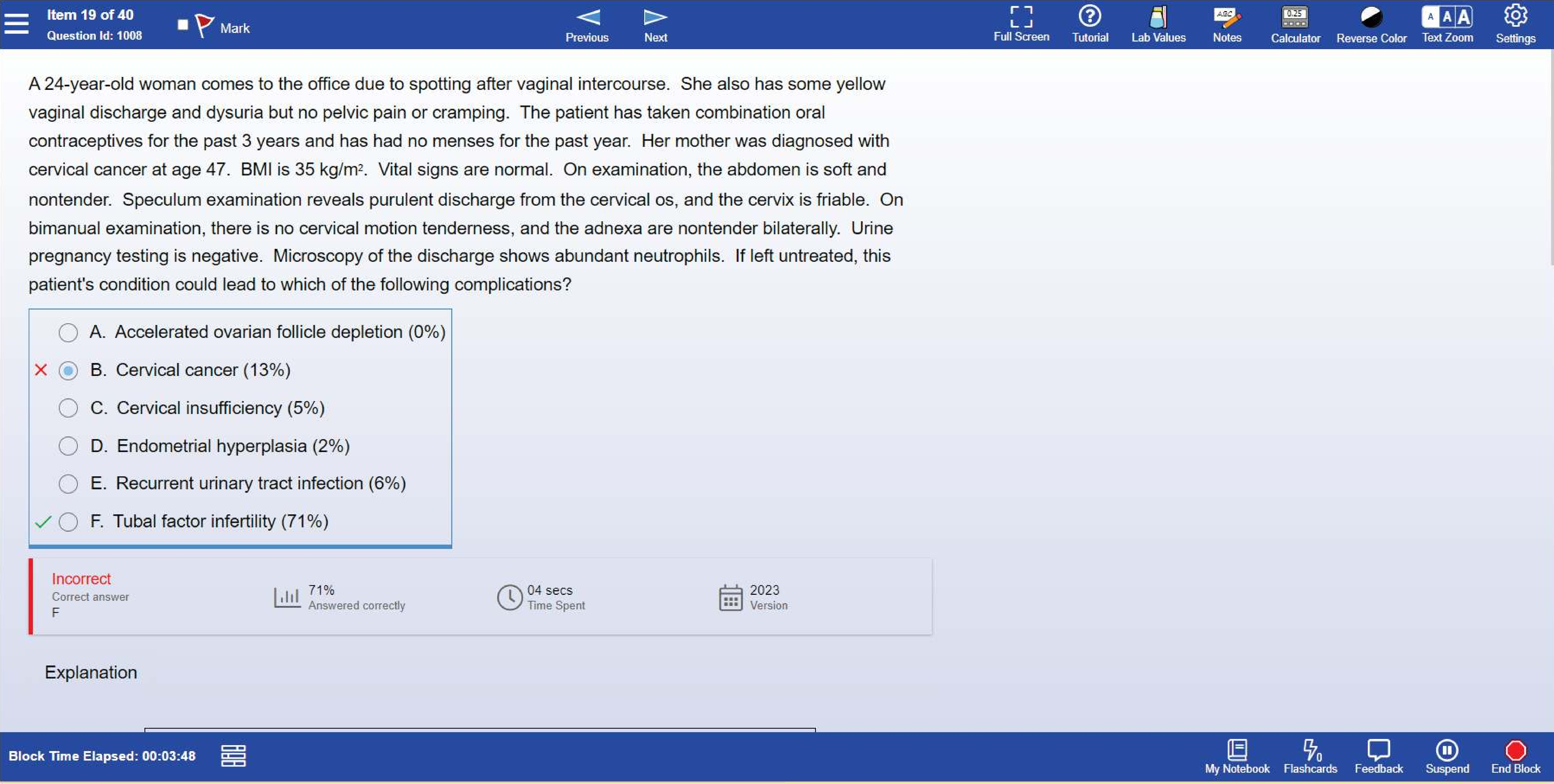
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○ A. Accelerated ovarian follicle depletion (0%)

✗ ● B. Cervical cancer (13%)

○ C. Cervical insufficiency (5%)

○ D. Endometrial hyperplasia (2%)

○ E. Recurrent urinary tract infection (6%)

✓ ○ F. Tubal factor infertility (71%)

Incorrect
Correct answer
F

71%
Answered correctly

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Explanation

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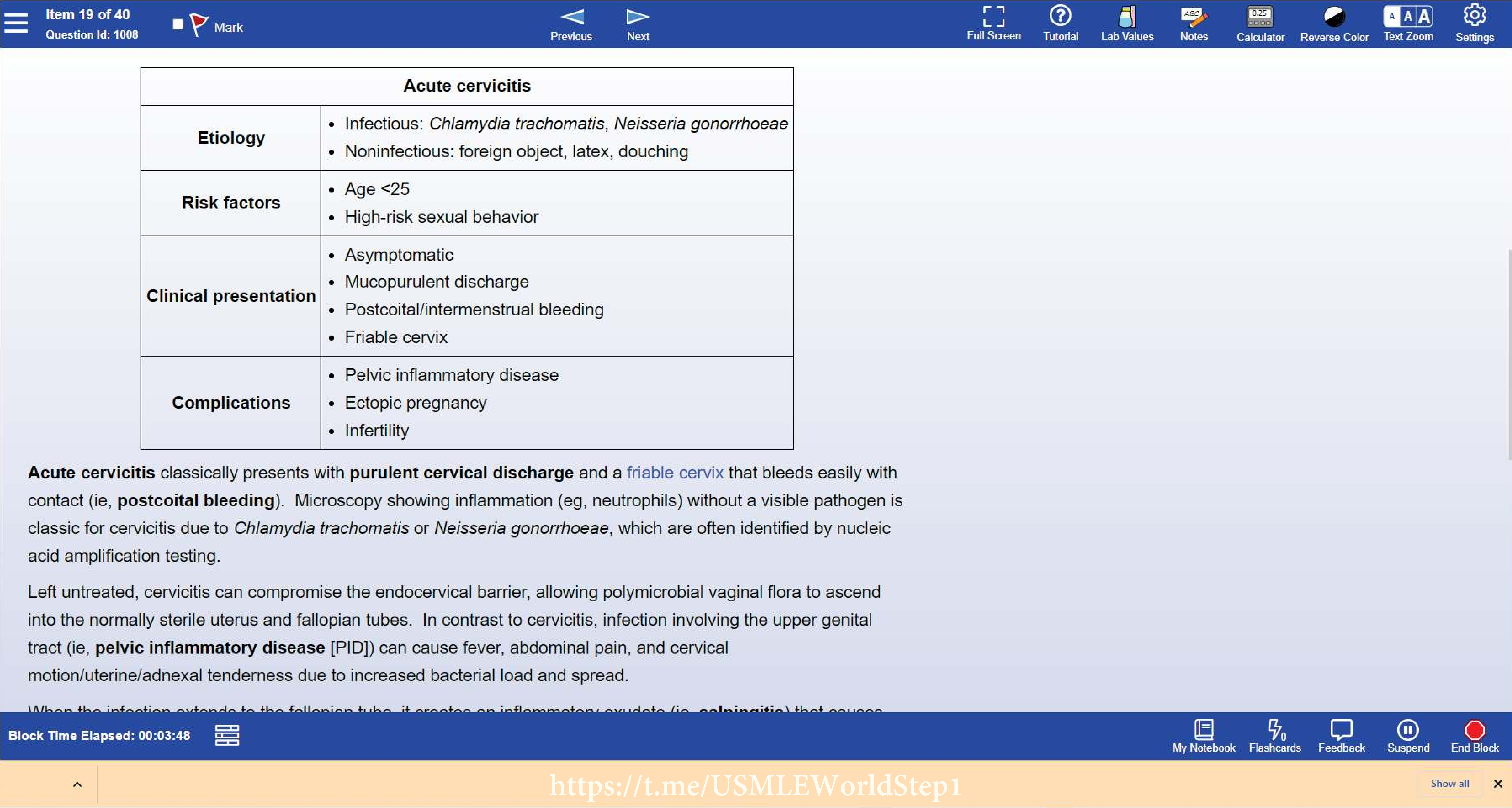
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Acute cervicitis	
Etiology	- Infectious: *Chlamydia trachomatis*, *Neisseria gonorrhoeae* - Noninfectious: foreign object, latex, douching
Risk factors	- Age <25 - High-risk sexual behavior
Clinical presentation	- Asymptomatic - Mucopurulent discharge - Postcoital/intermenstrual bleeding - Friable cervix
Complications	- Pelvic inflammatory disease - Ectopic pregnancy - Infertility

Acute cervicitis classically presents with **purulent cervical discharge** and a friable cervix that bleeds easily with contact (ie, **postcoital bleeding**). Microscopy showing inflammation (eg, neutrophils) without a visible pathogen is classic for cervicitis due to *Chlamydia trachomatis* or *Neisseria gonorrhoeae*, which are often identified by nucleic acid amplification testing.

Left untreated, cervicitis can compromise the endocervical barrier, allowing polymicrobial vaginal flora to ascend into the normally sterile uterus and fallopian tubes. In contrast to cervicitis, infection involving the upper genital tract (ie, **pelvic inflammatory disease** [PID]) can cause fever, abdominal pain, and cervical motion/uterine/adnexal tenderness due to increased bacterial load and spread.

When the infection extends to the fallopian tube, it creates an inflammatory exudate (ie, **salpingitis**) that causes

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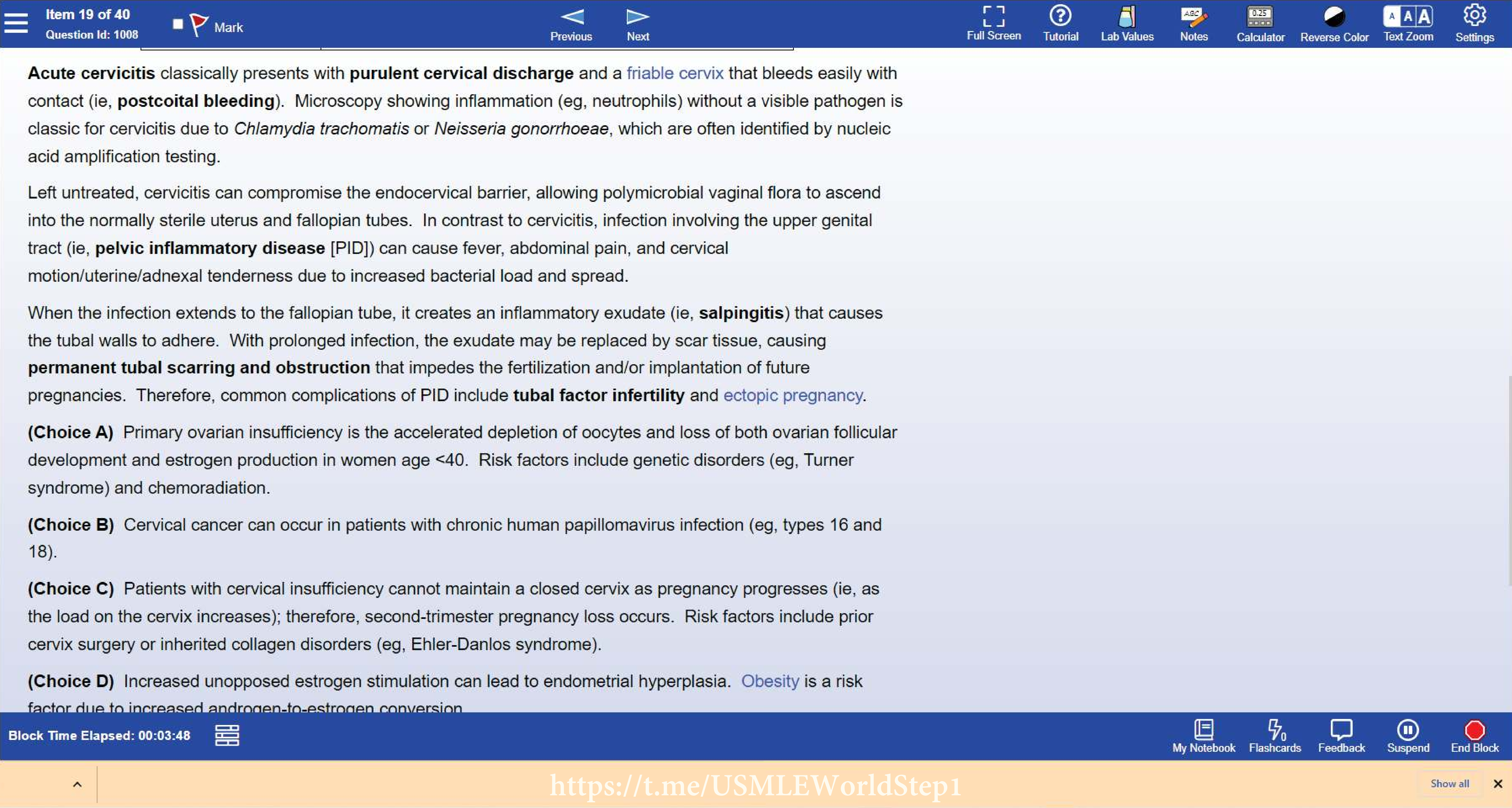

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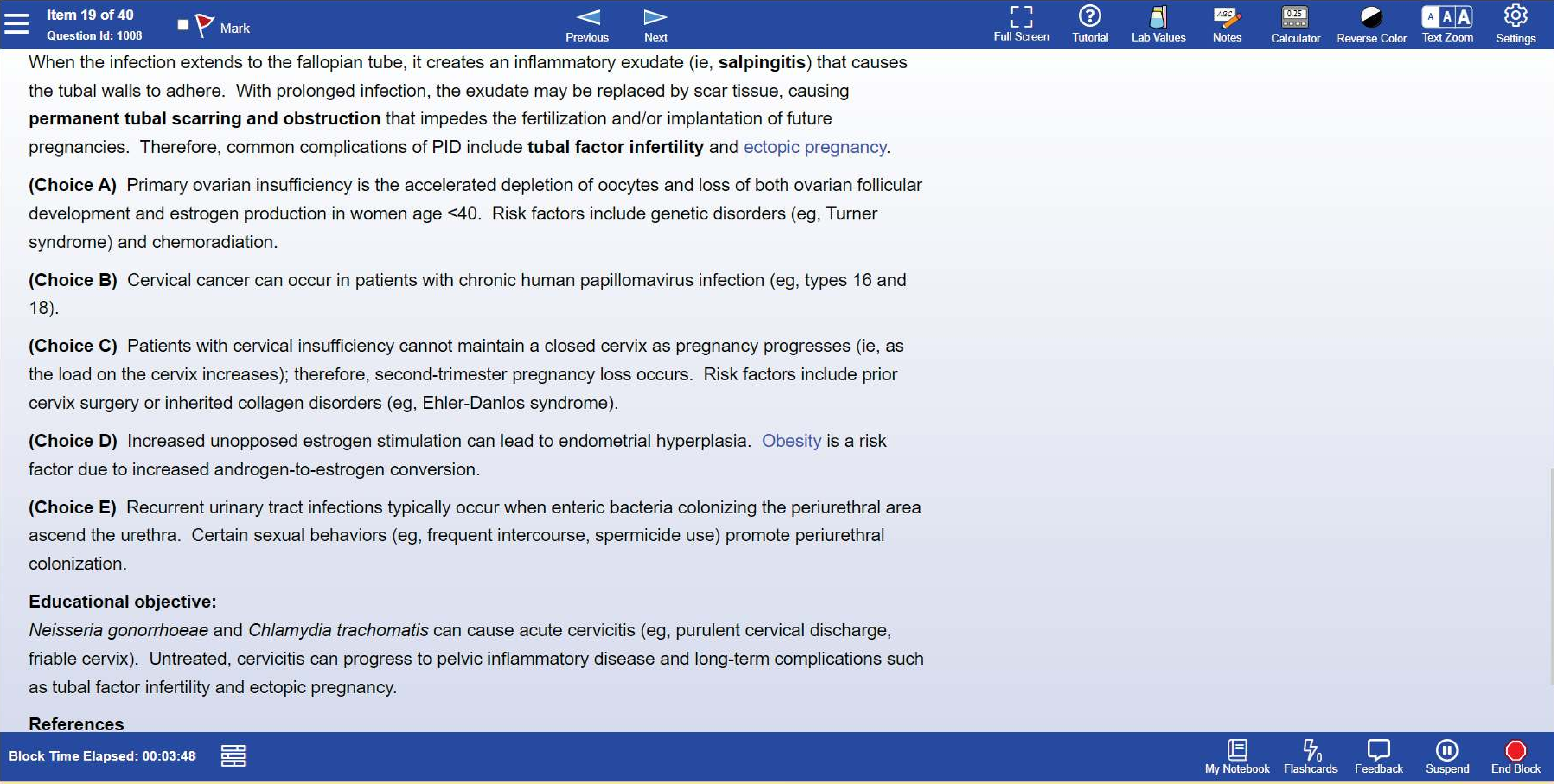
When the infection extends to the fallopian tube, it creates an inflammatory exudate (ie, **salpingitis**) that causes the tubal walls to adhere. With prolonged infection, the exudate may be replaced by scar tissue, causing **permanent tubal scarring and obstruction** that impedes the fertilization and/or implantation of future pregnancies. Therefore, common complications of PID include **tubal factor infertility** and ectopic pregnancy.

(Choice A) Primary ovarian insufficiency is the accelerated depletion of oocytes and loss of both ovarian follicular development and estrogen production in women age <40. Risk factors include genetic disorders (eg, Turner syndrome) and chemoradiation.

(Choice B) Cervical cancer can occur in patients with chronic human papillomavirus infection (eg, types 16 and 18).

(Choice C) Patients with cervical insufficiency cannot maintain a closed cervix as pregnancy progresses (ie, as the load on the cervix increases); therefore, second-trimester pregnancy loss occurs. Risk factors include prior cervix surgery or inherited collagen disorders (eg, Ehler-Danlos syndrome).

(Choice D) Increased unopposed estrogen stimulation can lead to endometrial hyperplasia. Obesity is a risk factor due to increased androgen-to-estrogen conversion.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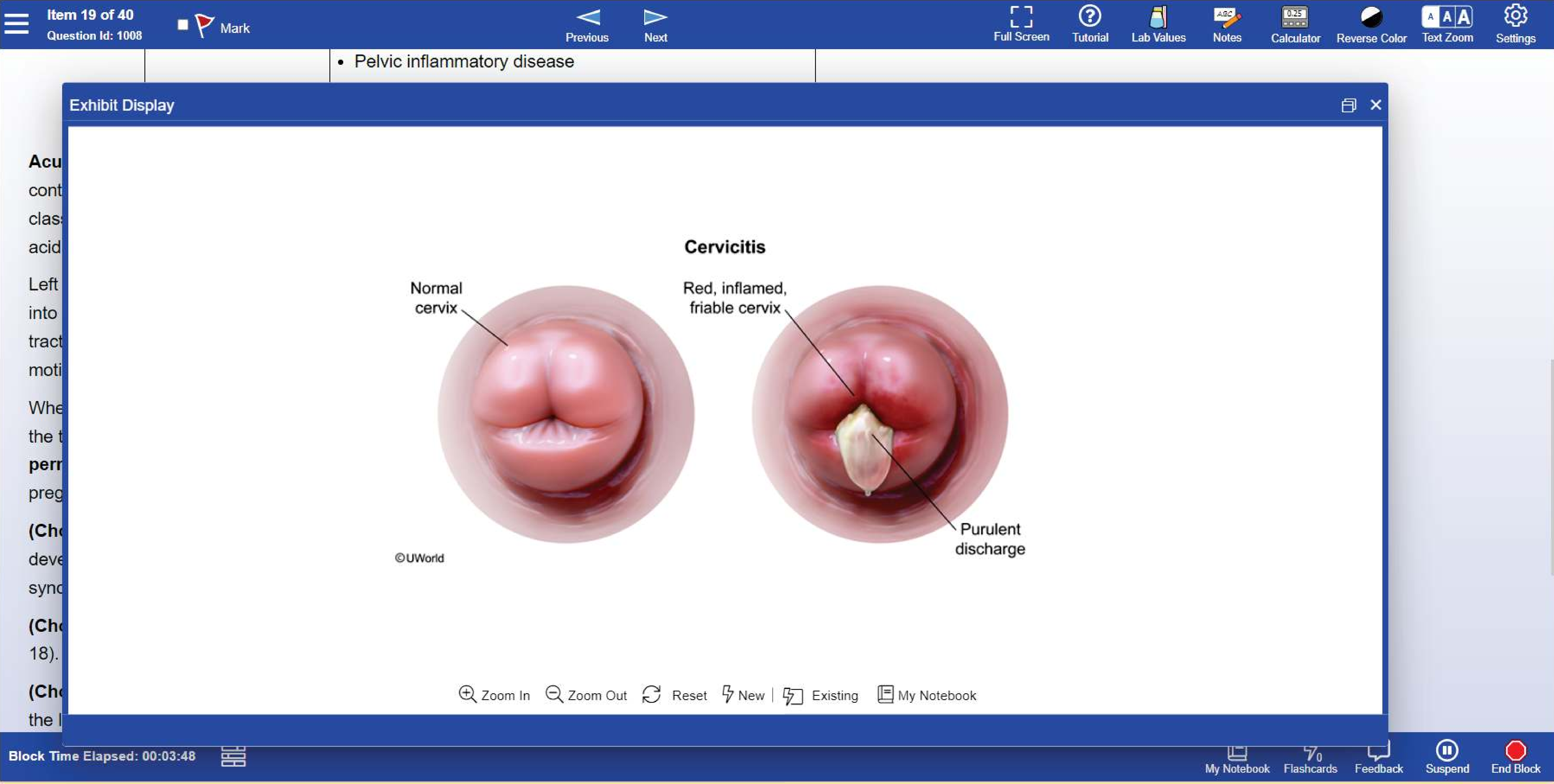
(Choice D) Increased unopposed estrogen stimulation can lead to endometrial hyperplasia. Obesity is a risk factor due to increased androgen-to-estrogen conversion.

(Choice E) Recurrent urinary tract infections typically occur when enteric bacteria colonizing the periurethral area ascend the urethra. Certain sexual behaviors (eg, frequent intercourse, spermicide use) promote periurethral colonization.

Educational objective:

Neisseria gonorrhoeae and *Chlamydia trachomatis* can cause acute cervicitis (eg, purulent cervical discharge, friable cervix). Untreated, cervicitis can progress to pelvic inflammatory disease and long-term complications such as tubal factor infertility and ectopic pregnancy.

References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Cervicitis

Normal cervix
Red, inflamed, friable cervix
Purulent discharge

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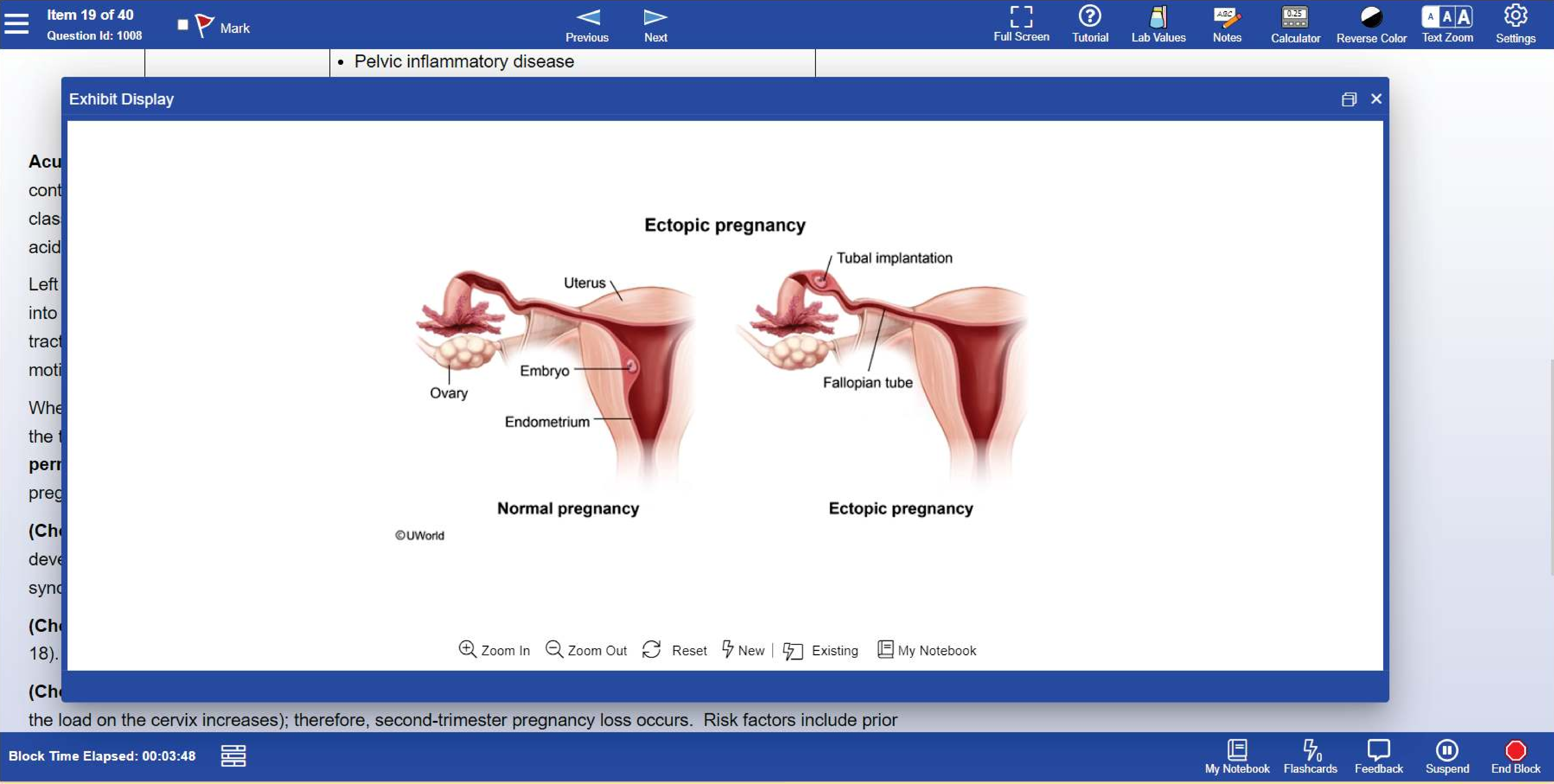
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Tubal implantation
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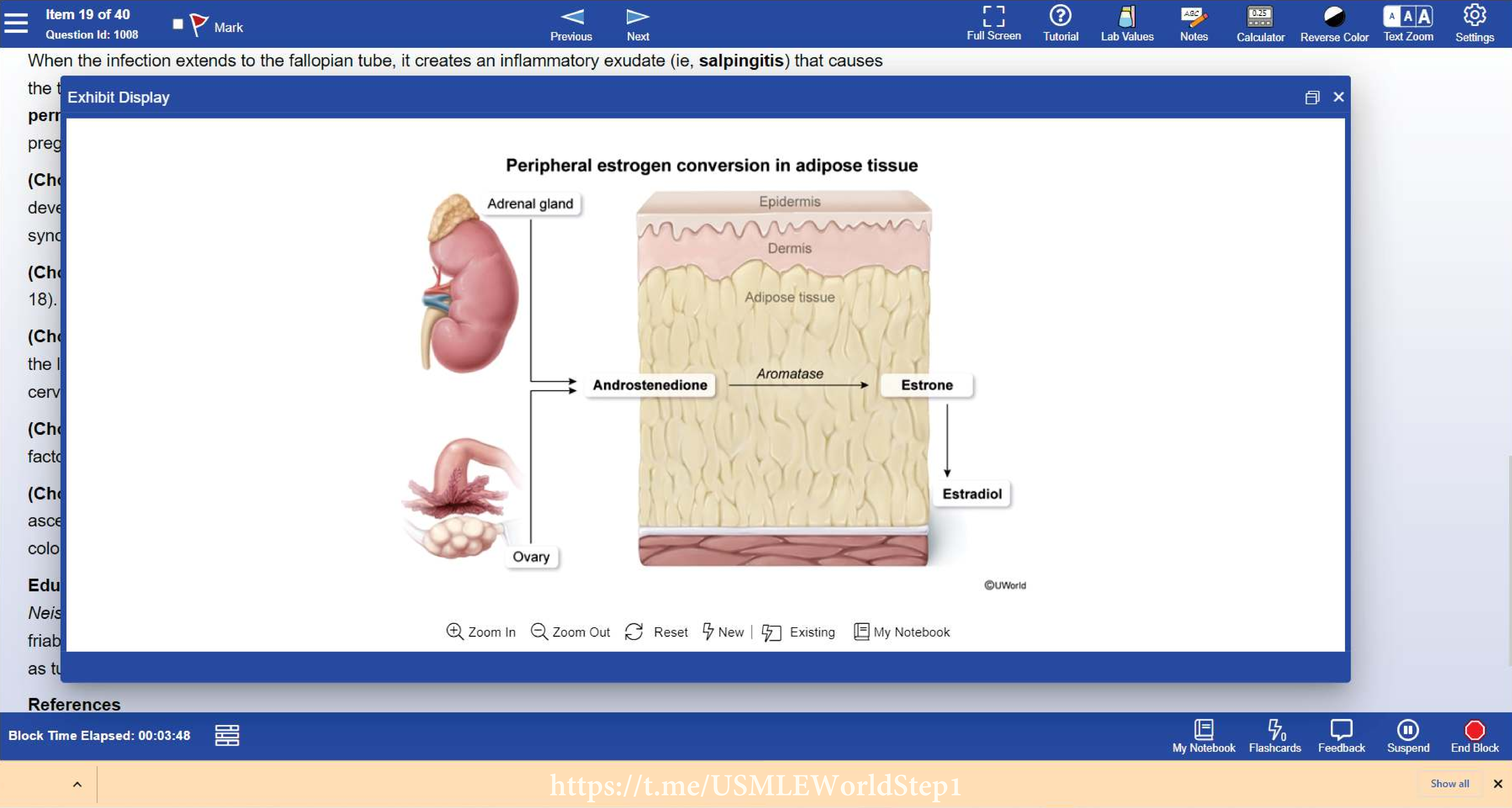

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Peripheral estrogen conversion in adipose tissue

Adrenal gland
Ovary
Epidermis
Dermis
Adipose tissue
Androstenedione
Aromatase
Estrone
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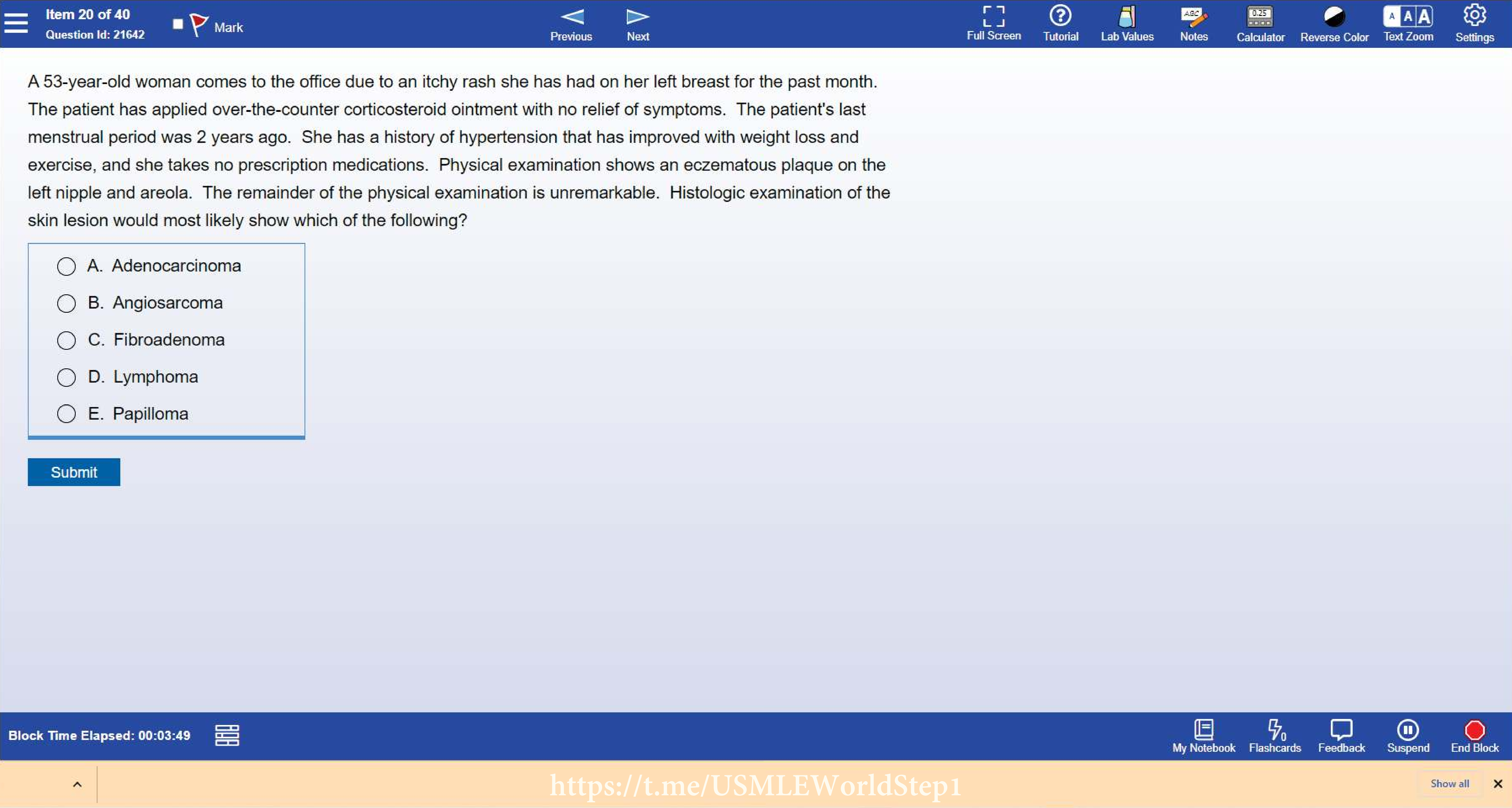
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A 53-year-old woman comes to the office due to an itchy rash she has had on her left breast for the past month. The patient has applied over-the-counter corticosteroid ointment with no relief of symptoms. The patient's last menstrual period was 2 years ago. She has a history of hypertension that has improved with weight loss and exercise, and she takes no prescription medications. Physical examination shows an eczematous plaque on the left nipple and areola. The remainder of the physical examination is unremarkable. Histologic examination of the skin lesion would most likely show which of the following?

○ A. Adenocarcinoma
○ B. Angiosarcoma
○ C. Fibroadenoma
○ D. Lymphoma
○ E. Papilloma

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✓ ○ A. Adenocarcinoma (52%)
✗ ● B. Angiosarcoma (7%)
○ C. Fibroadenoma (13%)
○ D. Lymphoma (3%)
○ E. Papilloma (23%)

Incorrect
Correct answer
A

52%
Answered correctly

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Explanation

Paget disease of the breast

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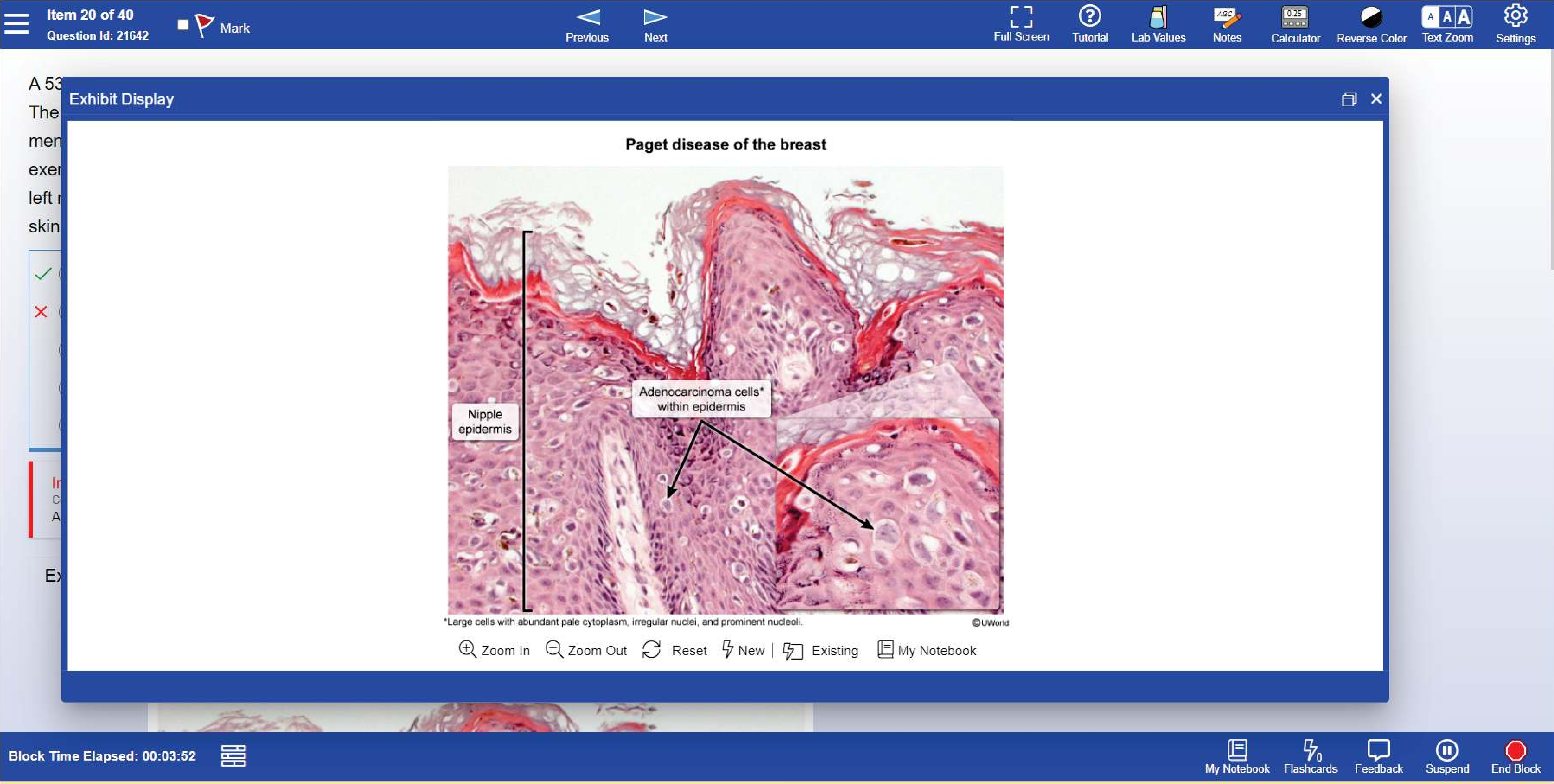
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Paget disease of the breast

Nipple epidermis
Adenocarcinoma cells* within epidermis

*Large cells with abundant pale cytoplasm, irregular nuclei, and prominent nucleoli.

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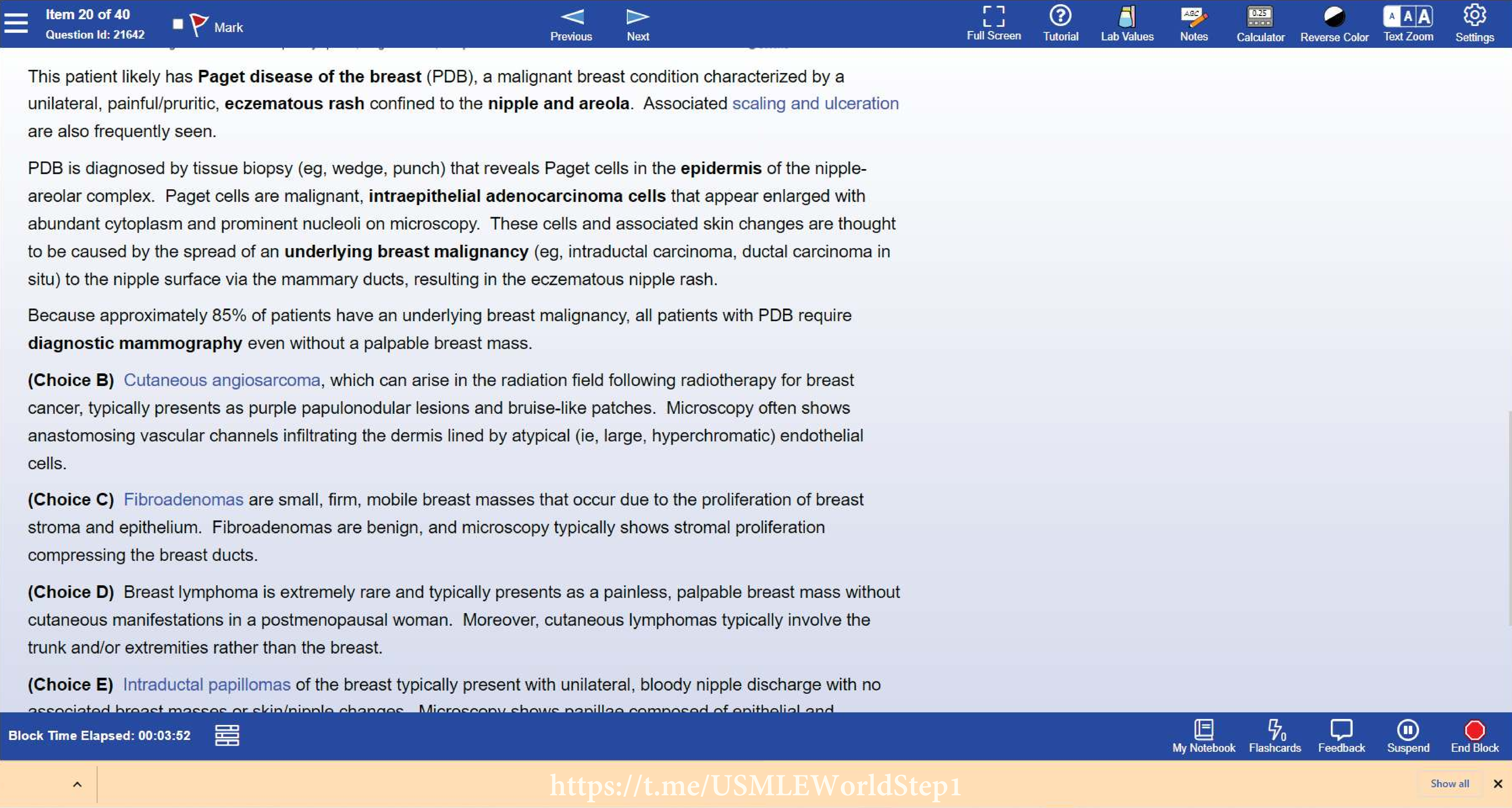


This patient likely has **Paget disease of the breast** (PDB), a malignant breast condition characterized by a unilateral, painful/pruritic, **eczematous rash** confined to the **nipple and areola**. Associated scaling and ulceration are also frequently seen.

PDB is diagnosed by tissue biopsy (eg, wedge, punch) that reveals Paget cells in the **epidermis** of the nipple-areolar complex. Paget cells are malignant, **intraepithelial adenocarcinoma cells** that appear enlarged with abundant cytoplasm and prominent nucleoli on microscopy. These cells and associated skin changes are thought to be caused by the spread of an **underlying breast malignancy** (eg, intraductal carcinoma, ductal carcinoma in situ) to the nipple surface via the mammary ducts, resulting in the eczematous nipple rash.

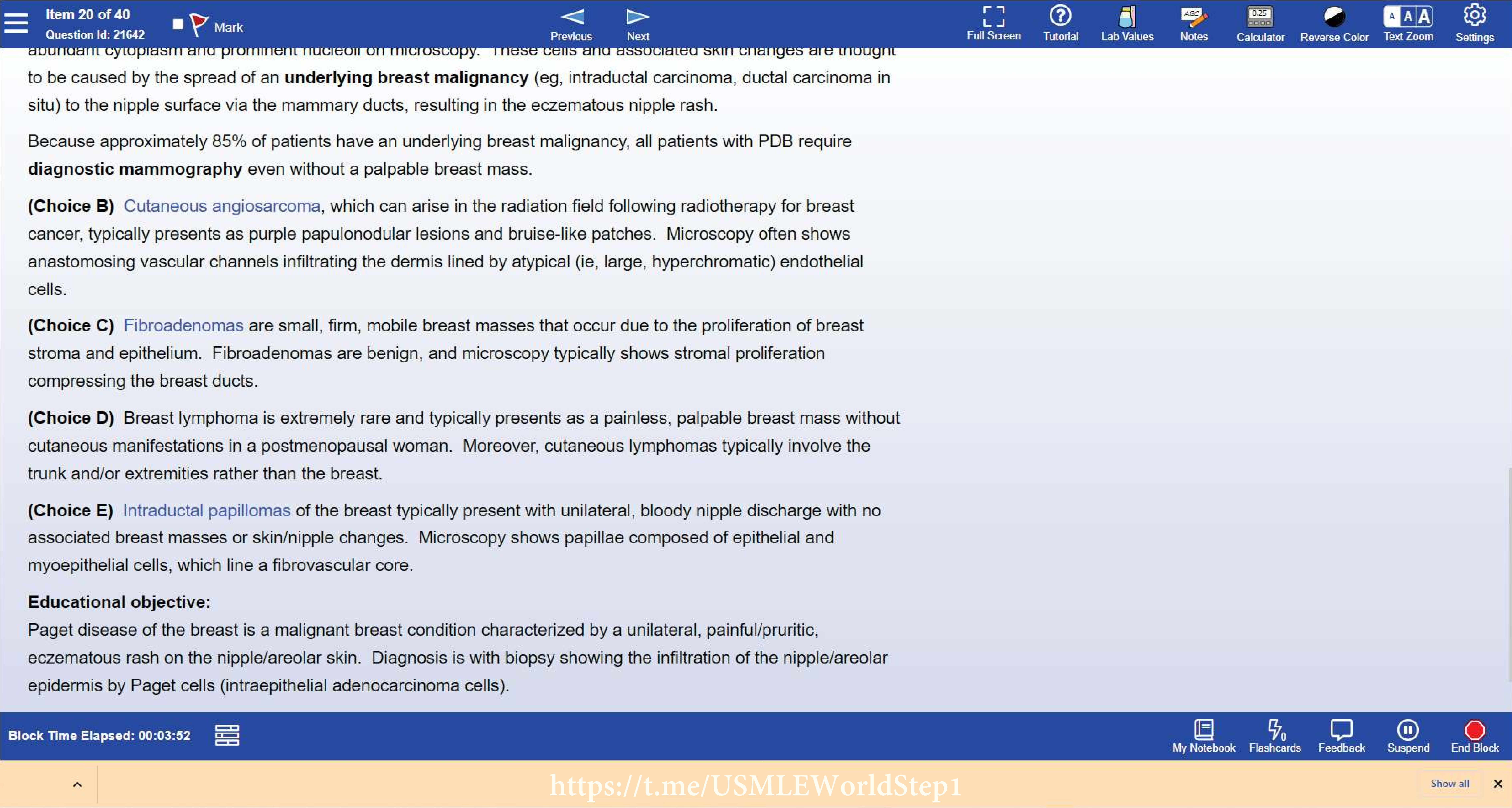
Because approximately 85% of patients have an underlying breast malignancy, all patients with PDB require **diagnostic mammography** even without a palpable breast mass.

(Choice B) Cutaneous angiosarcoma, which can arise in the radiation field following radiotherapy for breast cancer, typically presents as purple papulonodular lesions and bruise-like patches. Microscopy often shows anastomosing vascular channels infiltrating the dermis lined by atypical (ie, large, hyperchromatic) endothelial cells.

(Choice C) Fibroadenomas are small, firm, mobile breast masses that occur due to the proliferation of breast stroma and epithelium. Fibroadenomas are benign, and microscopy typically shows stromal proliferation compressing the breast ducts.

(Choice D) Breast lymphoma is extremely rare and typically presents as a painless, palpable breast mass without cutaneous manifestations in a postmenopausal woman. Moreover, cutaneous lymphomas typically involve the trunk and/or extremities rather than the breast.

(Choice E) Intraductal papillomas of the breast typically present with unilateral, bloody nipple discharge with no associated breast masses or skin/nipple changes. Microscopy shows papillae composed of epithelial and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abundant cytoplasm and prominent nucleoli on microscopy. These cells and associated skin changes are thought to be caused by the spread of an **underlying breast malignancy** (eg, intraductal carcinoma, ductal carcinoma in situ) to the nipple surface via the mammary ducts, resulting in the eczematous nipple rash.

Because approximately 85% of patients have an underlying breast malignancy, all patients with PDB require **diagnostic mammography** even without a palpable breast mass.

(Choice B) Cutaneous angiosarcoma, which can arise in the radiation field following radiotherapy for breast cancer, typically presents as purple papulonodular lesions and bruise-like patches. Microscopy often shows anastomosing vascular channels infiltrating the dermis lined by atypical (ie, large, hyperchromatic) endothelial cells.

(Choice C) Fibroadenomas are small, firm, mobile breast masses that occur due to the proliferation of breast stroma and epithelium. Fibroadenomas are benign, and microscopy typically shows stromal proliferation compressing the breast ducts.

(Choice D) Breast lymphoma is extremely rare and typically presents as a painless, palpable breast mass without cutaneous manifestations in a postmenopausal woman. Moreover, cutaneous lymphomas typically involve the trunk and/or extremities rather than the breast.

(Choice E) Intraductal papillomas of the breast typically present with unilateral, bloody nipple discharge with no associated breast masses or skin/nipple changes. Microscopy shows papillae composed of epithelial and myoepithelial cells, which line a fibrovascular core.

Educational objective:
Paget disease of the breast is a malignant breast condition characterized by a unilateral, painful/pruritic, eczematous rash on the nipple/areolar skin. Diagnosis is with biopsy showing the infiltration of the nipple/areolar epidermis by Paget cells (intraepithelial adenocarcinoma cells).

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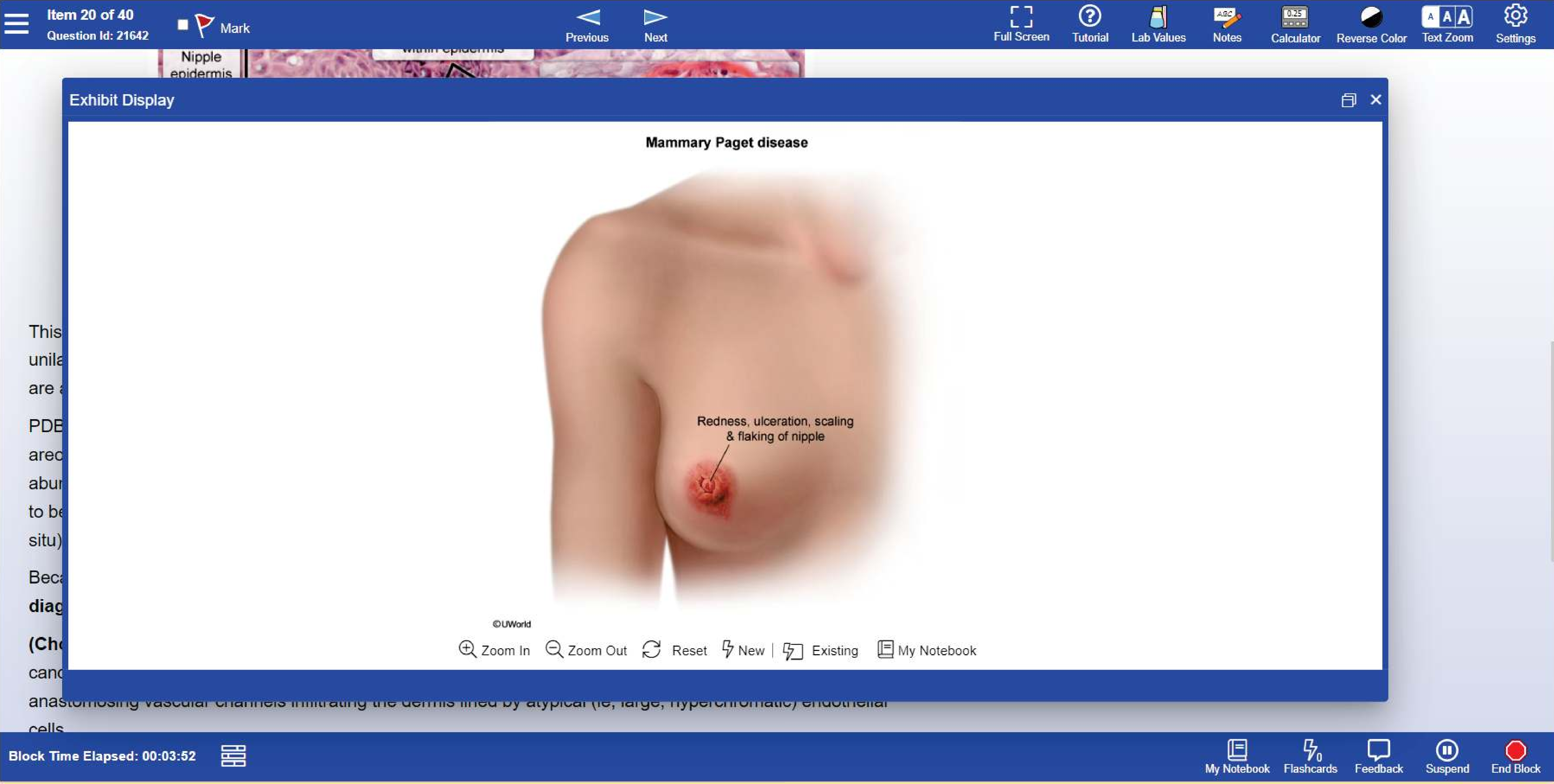
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Nipple epidermis
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Mammary Paget disease

Redness, ulceration, scaling & flaking of nipple

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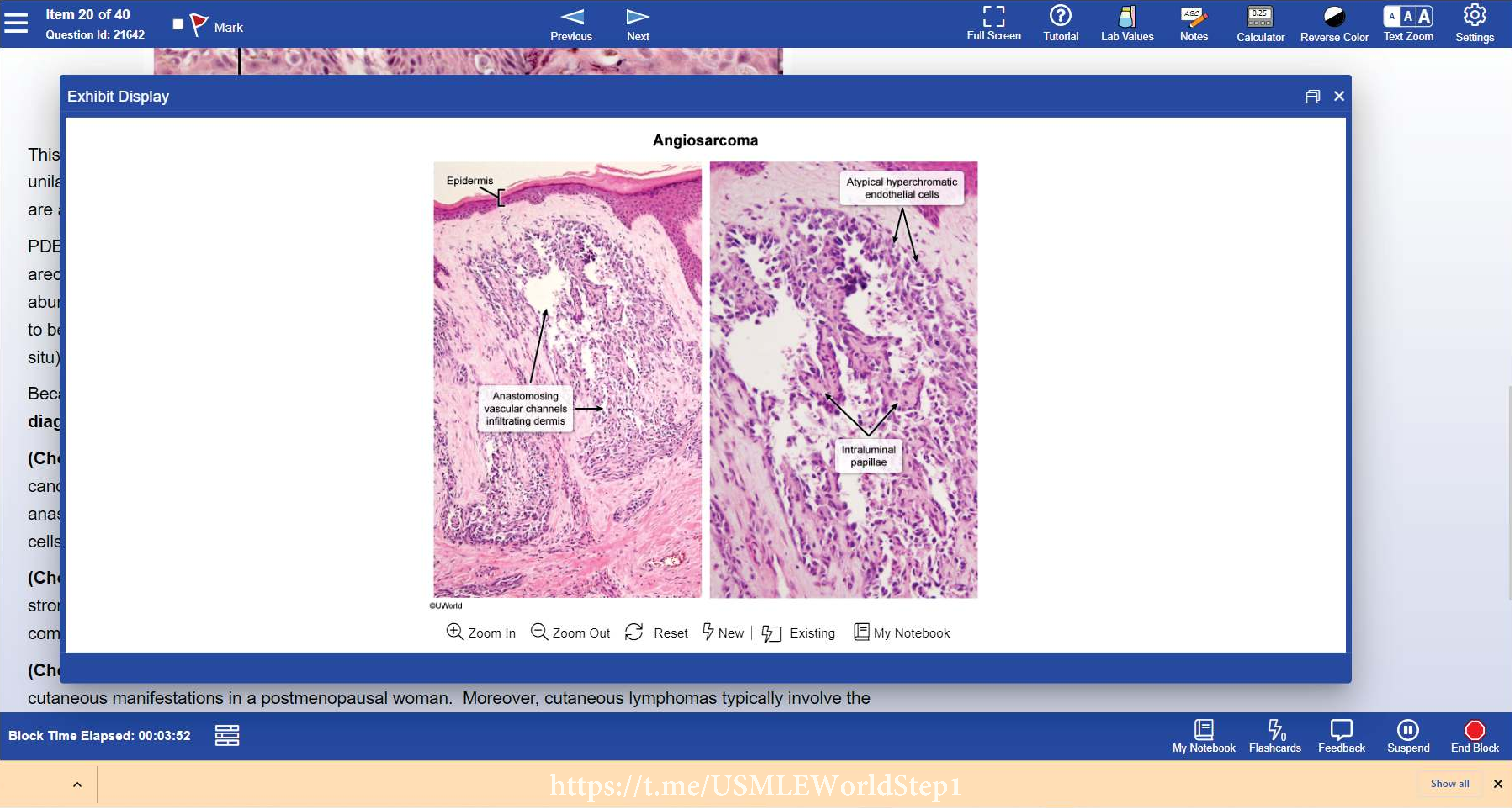
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Angiosarcoma

Epidermis
Anastomosing vascular channels infiltrating dermis
Atypical hyperchromatic endothelial cells
Intraluminal papillae
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cutaneous manifestations in a postmenopausal woman. Moreover, cutaneous lymphomas typically involve the

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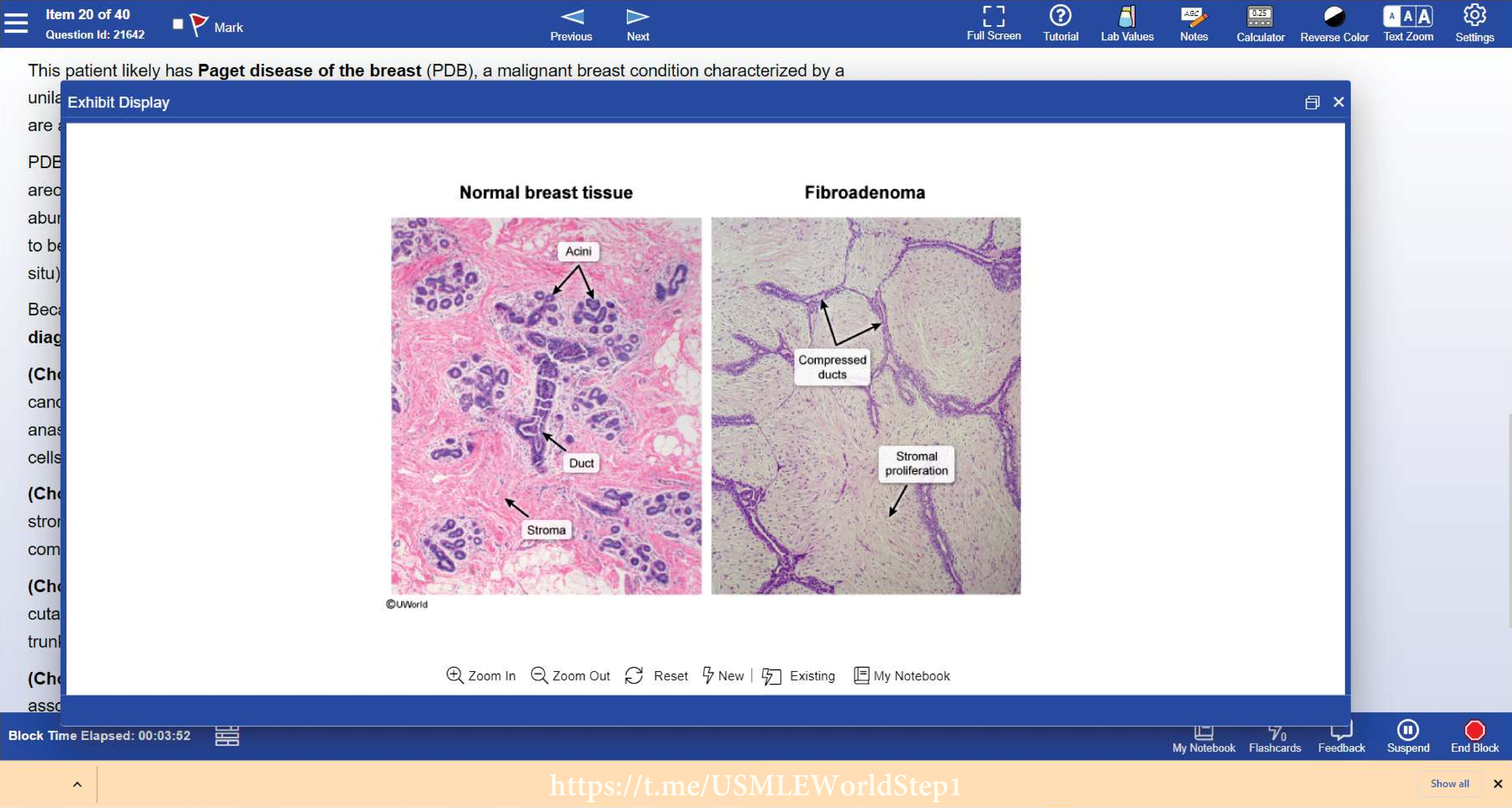
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This patient likely has **Paget disease of the breast** (PDB), a malignant breast condition characterized by a

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Normal breast tissue

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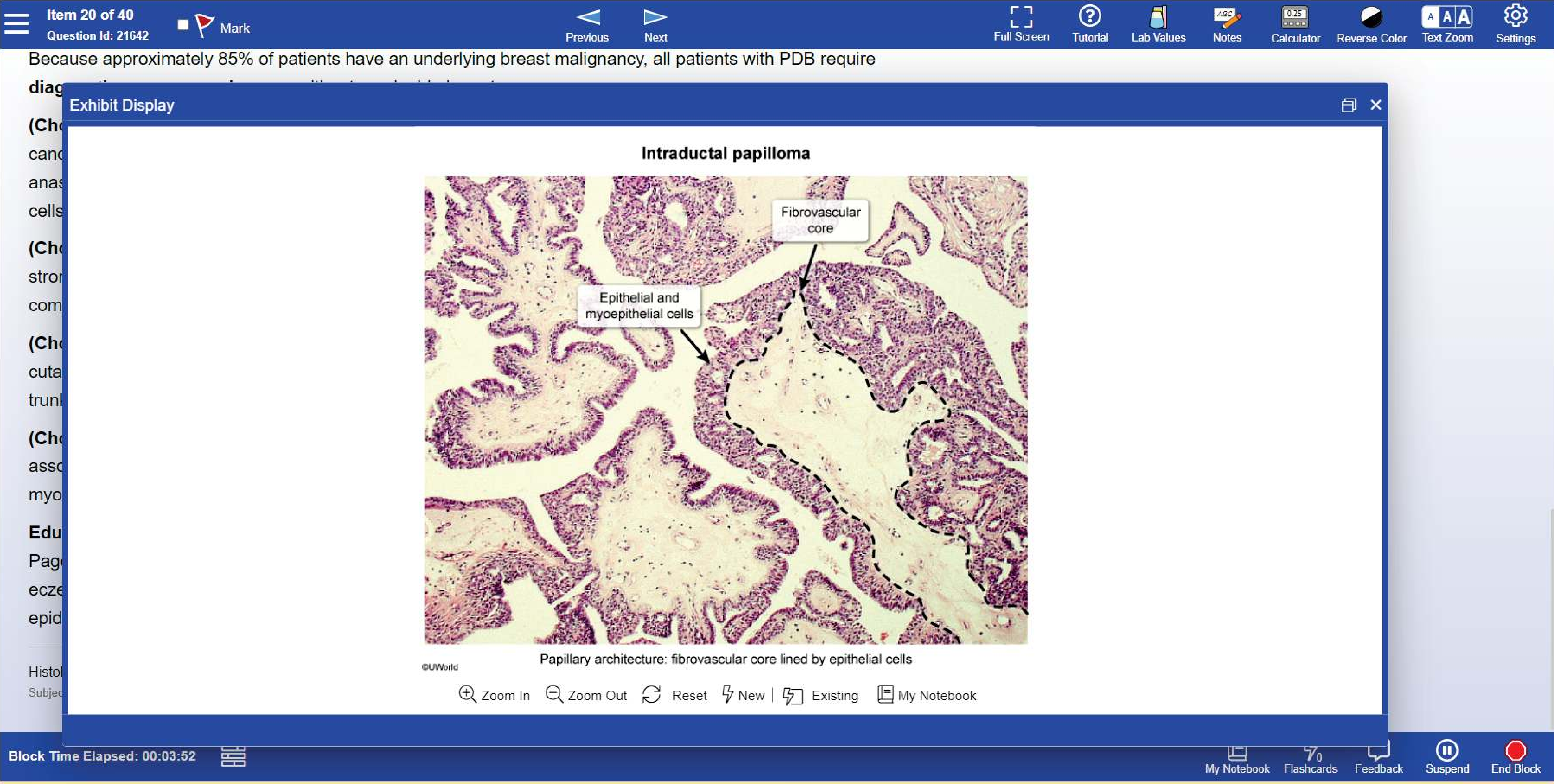

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Because approximately 85% of patients have an underlying breast malignancy, all patients with PDB require

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Intraductal papilloma

Fibrovascular core
Epithelial and myoepithelial cells

Papillary architecture: fibrovascular core lined by epithelial cells

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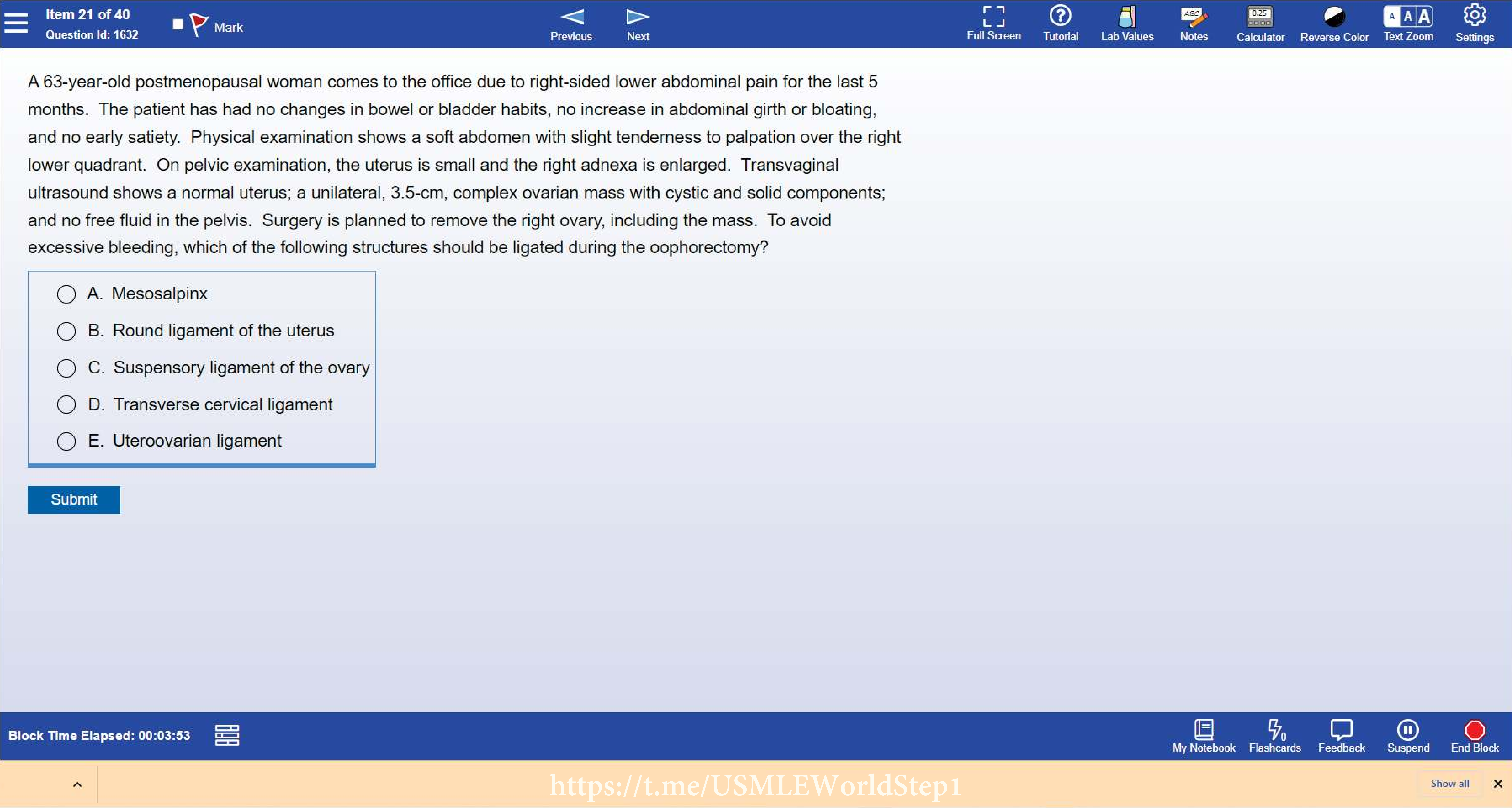
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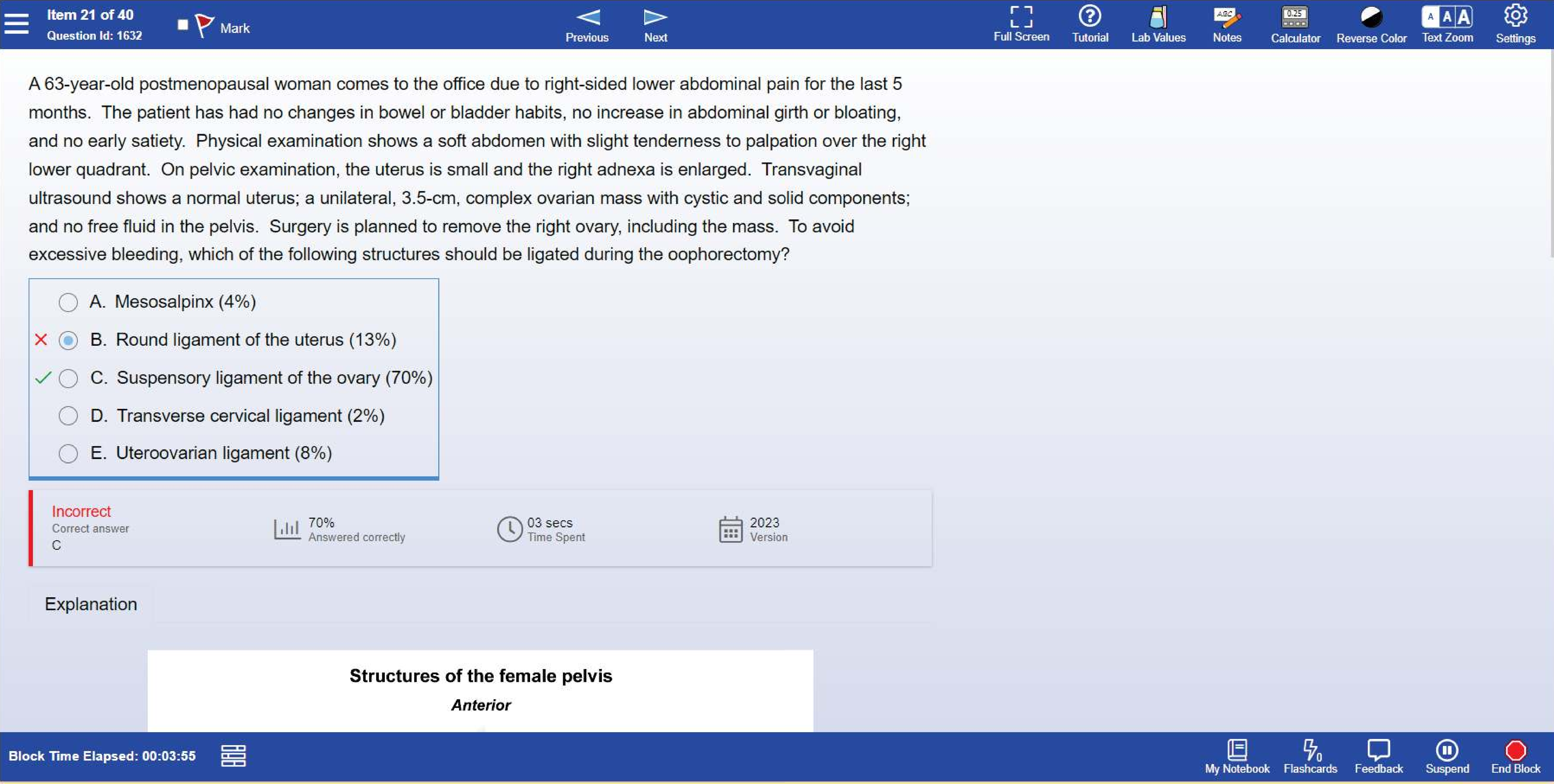
A 63-year-old postmenopausal woman comes to the office due to right-sided lower abdominal pain for the last 5 months. The patient has had no changes in bowel or bladder habits, no increase in abdominal girth or bloating, and no early satiety. Physical examination shows a soft abdomen with slight tenderness to palpation over the right lower quadrant. On pelvic examination, the uterus is small and the right adnexa is enlarged. Transvaginal ultrasound shows a normal uterus; a unilateral, 3.5-cm, complex ovarian mass with cystic and solid components; and no free fluid in the pelvis. Surgery is planned to remove the right ovary, including the mass. To avoid excessive bleeding, which of the following structures should be ligated during the oophorectomy?

○ A. Mesosalpinx
○ B. Round ligament of the uterus
○ C. Suspensory ligament of the ovary
○ D. Transverse cervical ligament
○ E. Uteroovarian ligament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- ○ A. Mesosalpinx (4%)
- ✗ ● B. Round ligament of the uterus (13%)
- ✓ ○ C. Suspensory ligament of the ovary (70%)
- ○ D. Transverse cervical ligament (2%)
- ○ E. Uteroovarian ligament (8%)

Incorrect
Correct answer
C

70%
Answered correctly

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Explanation

Structures of the female pelvis

Anterior

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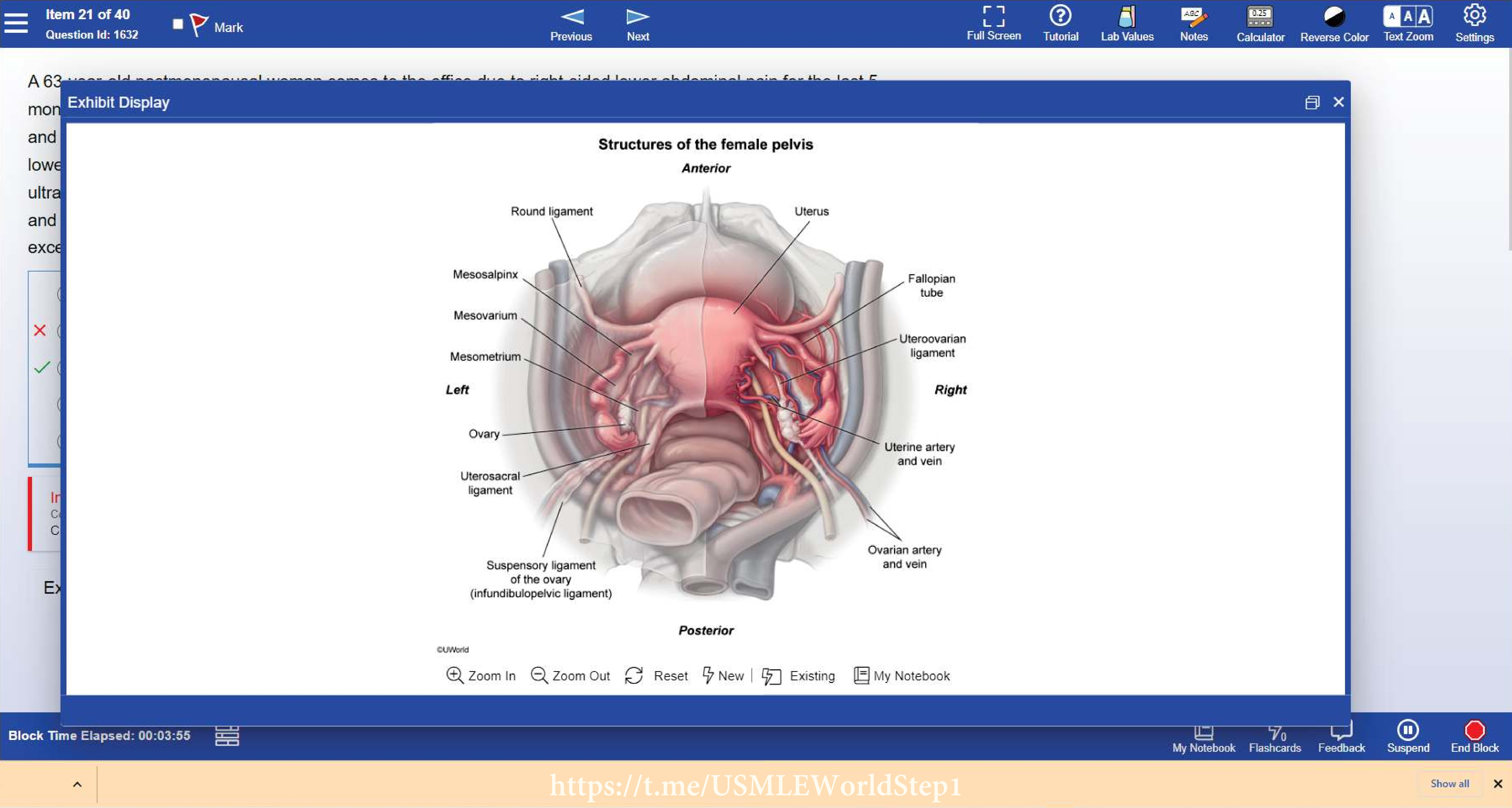
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Structures of the female pelvis

Anterior
Round ligament
Uterus
Mesosalpinx
Fallopian tube
Mesovarium
Uteroovarian ligament
Mesometrium
Left
Right
Ovary
Uterine artery and vein
Uterosacral ligament
Ovarian artery and vein
Suspensory ligament of the ovary (infundibulopelvic ligament)
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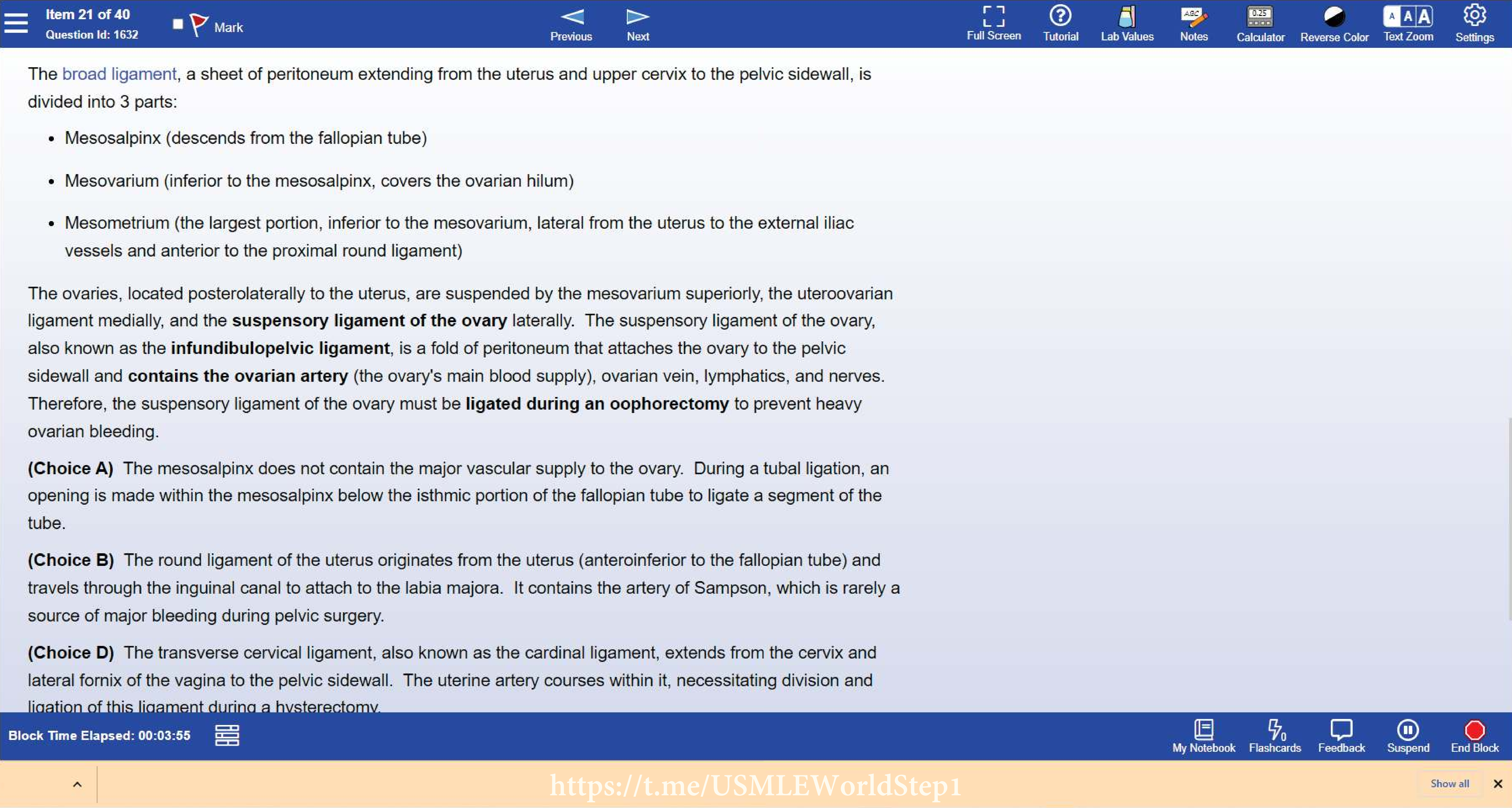
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The broad ligament, a sheet of peritoneum extending from the uterus and upper cervix to the pelvic sidewall, is divided into 3 parts:

- Mesosalpinx (descends from the fallopian tube)
- Mesovarium (inferior to the mesosalpinx, covers the ovarian hilum)
- Mesometrium (the largest portion, inferior to the mesovarium, lateral from the uterus to the external iliac vessels and anterior to the proximal round ligament)

The ovaries, located posterolaterally to the uterus, are suspended by the mesovarium superiorly, the uteroovarian ligament medially, and the **suspensory ligament of the ovary** laterally. The suspensory ligament of the ovary, also known as the **infundibulopelvic ligament**, is a fold of peritoneum that attaches the ovary to the pelvic sidewall and **contains the ovarian artery** (the ovary's main blood supply), ovarian vein, lymphatics, and nerves. Therefore, the suspensory ligament of the ovary must be **ligated during an oophorectomy** to prevent heavy ovarian bleeding.

(Choice A) The mesosalpinx does not contain the major vascular supply to the ovary. During a tubal ligation, an opening is made within the mesosalpinx below the isthmic portion of the fallopian tube to ligate a segment of the tube.

(Choice B) The round ligament of the uterus originates from the uterus (anteroinferior to the fallopian tube) and travels through the inguinal canal to attach to the labia majora. It contains the artery of Sampson, which is rarely a source of major bleeding during pelvic surgery.

(Choice D) The transverse cervical ligament, also known as the cardinal ligament, extends from the cervix and lateral fornix of the vagina to the pelvic sidewall. The uterine artery courses within it, necessitating division and ligation of this ligament during a hysterectomy.

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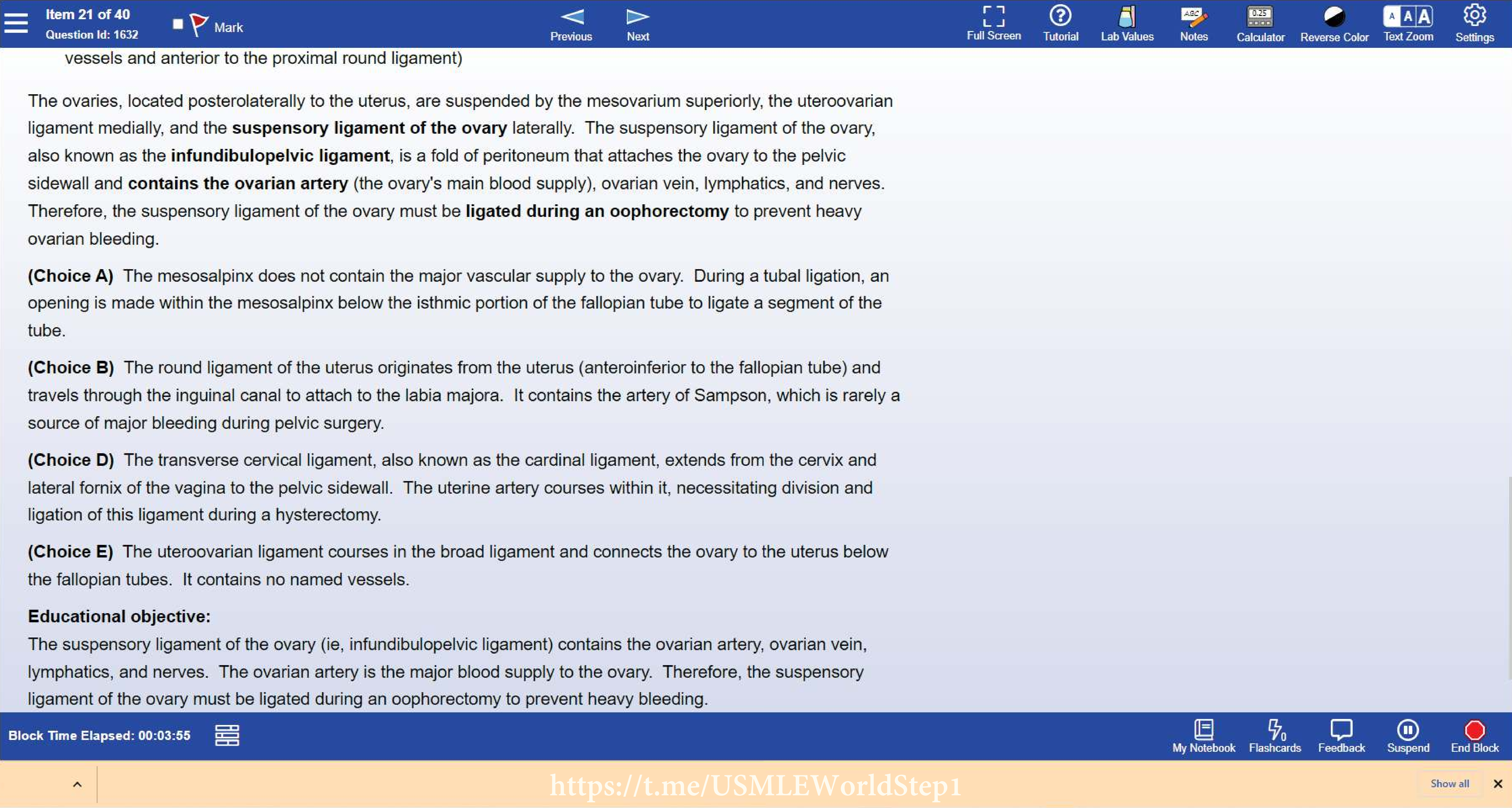
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vessels and anterior to the proximal round ligament)

The ovaries, located posterolaterally to the uterus, are suspended by the mesovarium superiorly, the uteroovarian ligament medially, and the **suspensory ligament of the ovary** laterally. The suspensory ligament of the ovary, also known as the **infundibulopelvic ligament**, is a fold of peritoneum that attaches the ovary to the pelvic sidewall and **contains the ovarian artery** (the ovary's main blood supply), ovarian vein, lymphatics, and nerves. Therefore, the suspensory ligament of the ovary must be **ligated during an oophorectomy** to prevent heavy ovarian bleeding.

(Choice A) The mesosalpinx does not contain the major vascular supply to the ovary. During a tubal ligation, an opening is made within the mesosalpinx below the isthmic portion of the fallopian tube to ligate a segment of the tube.

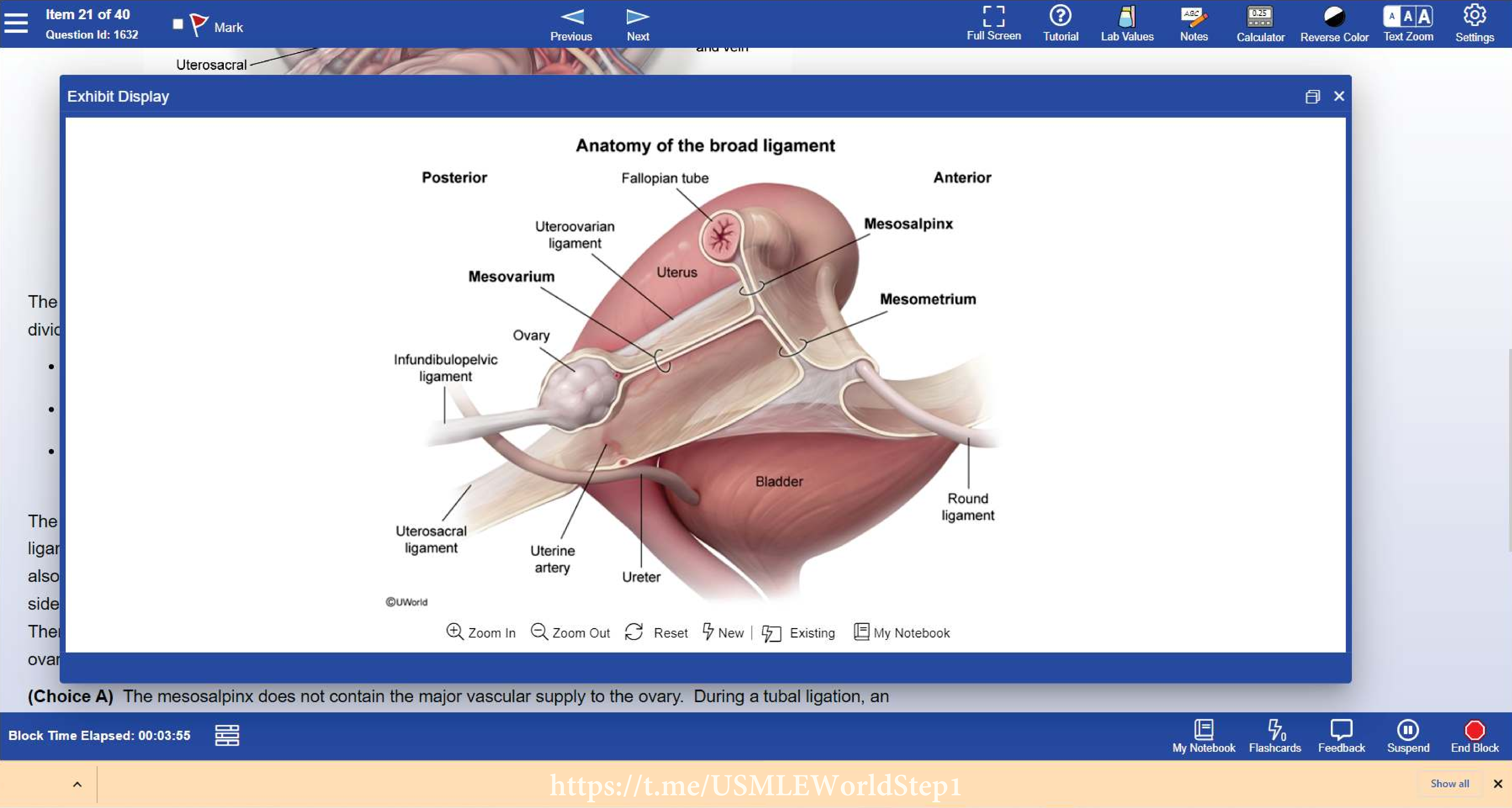
(Choice B) The round ligament of the uterus originates from the uterus (anteroinferior to the fallopian tube) and travels through the inguinal canal to attach to the labia majora. It contains the artery of Sampson, which is rarely a source of major bleeding during pelvic surgery.

(Choice D) The transverse cervical ligament, also known as the cardinal ligament, extends from the cervix and lateral fornix of the vagina to the pelvic sidewall. The uterine artery courses within it, necessitating division and ligation of this ligament during a hysterectomy.

(Choice E) The uteroovarian ligament courses in the broad ligament and connects the ovary to the uterus below the fallopian tubes. It contains no named vessels.

Educational objective:

The suspensory ligament of the ovary (ie, infundibulopelvic ligament) contains the ovarian artery, ovarian vein, lymphatics, and nerves. The ovarian artery is the major blood supply to the ovary. Therefore, the suspensory ligament of the ovary must be ligated during an oophorectomy to prevent heavy bleeding.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Uterosacral
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Fallopian tube
Uteroovarian ligament
Mesosalpinx
Uterus
Mesovarium
Mesometrium
Ovary
Infundibulopelvic ligament
Bladder
Round ligament
Uterosacral ligament
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Anatomy of the broad ligament

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(Choice A) The mesosalpinx does not contain the major vascular supply to the ovary. During a tubal ligation, an

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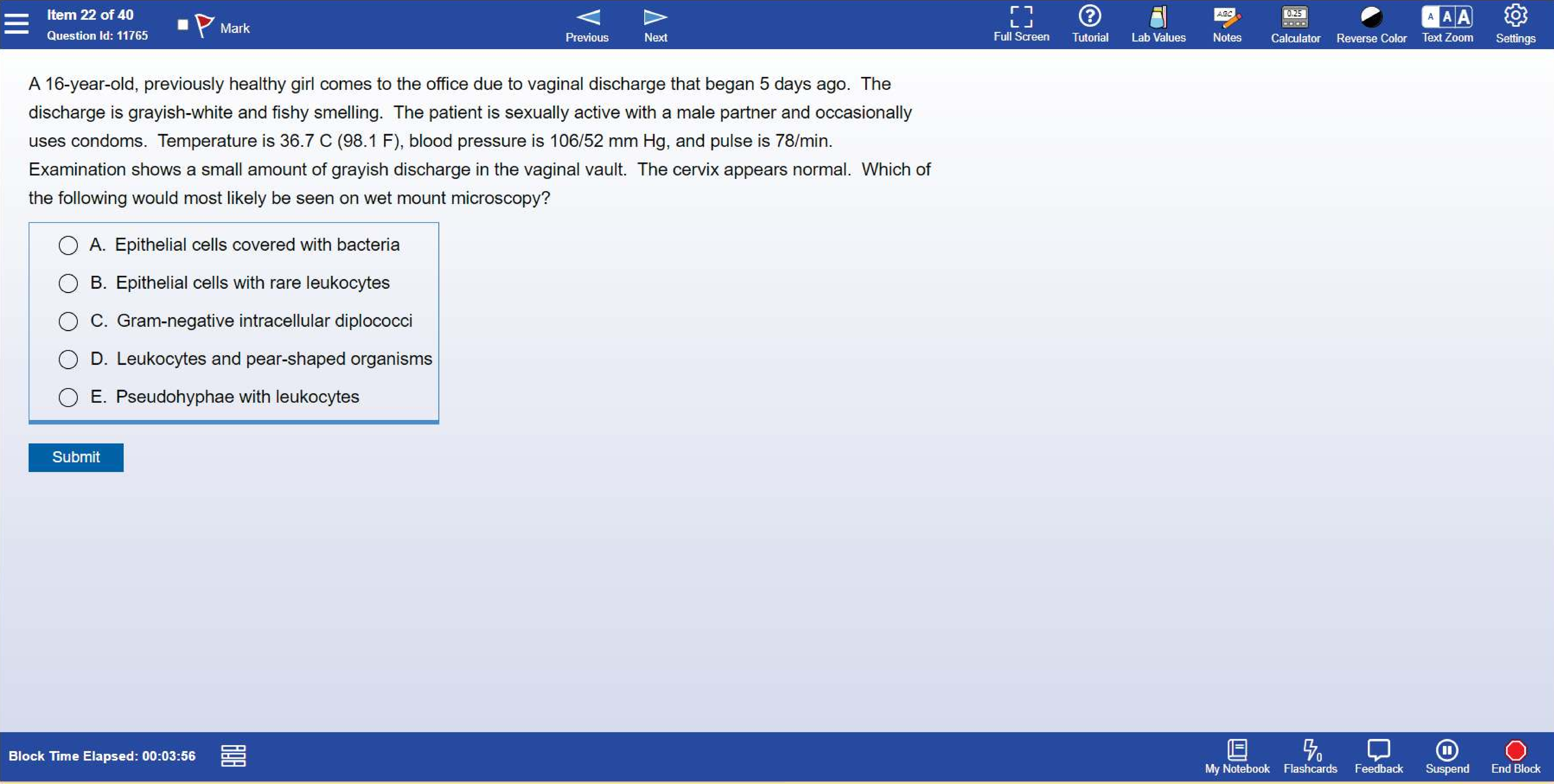
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A 16-year-old, previously healthy girl comes to the office due to vaginal discharge that began 5 days ago. The discharge is grayish-white and fishy smelling. The patient is sexually active with a male partner and occasionally uses condoms. Temperature is 36.7 C (98.1 F), blood pressure is 106/52 mm Hg, and pulse is 78/min. Examination shows a small amount of grayish discharge in the vaginal vault. The cervix appears normal. Which of the following would most likely be seen on wet mount microscopy?

○ A. Epithelial cells covered with bacteria
○ B. Epithelial cells with rare leukocytes
○ C. Gram-negative intracellular diplococci
○ D. Leukocytes and pear-shaped organisms
○ E. Pseudohyphae with leukocytes

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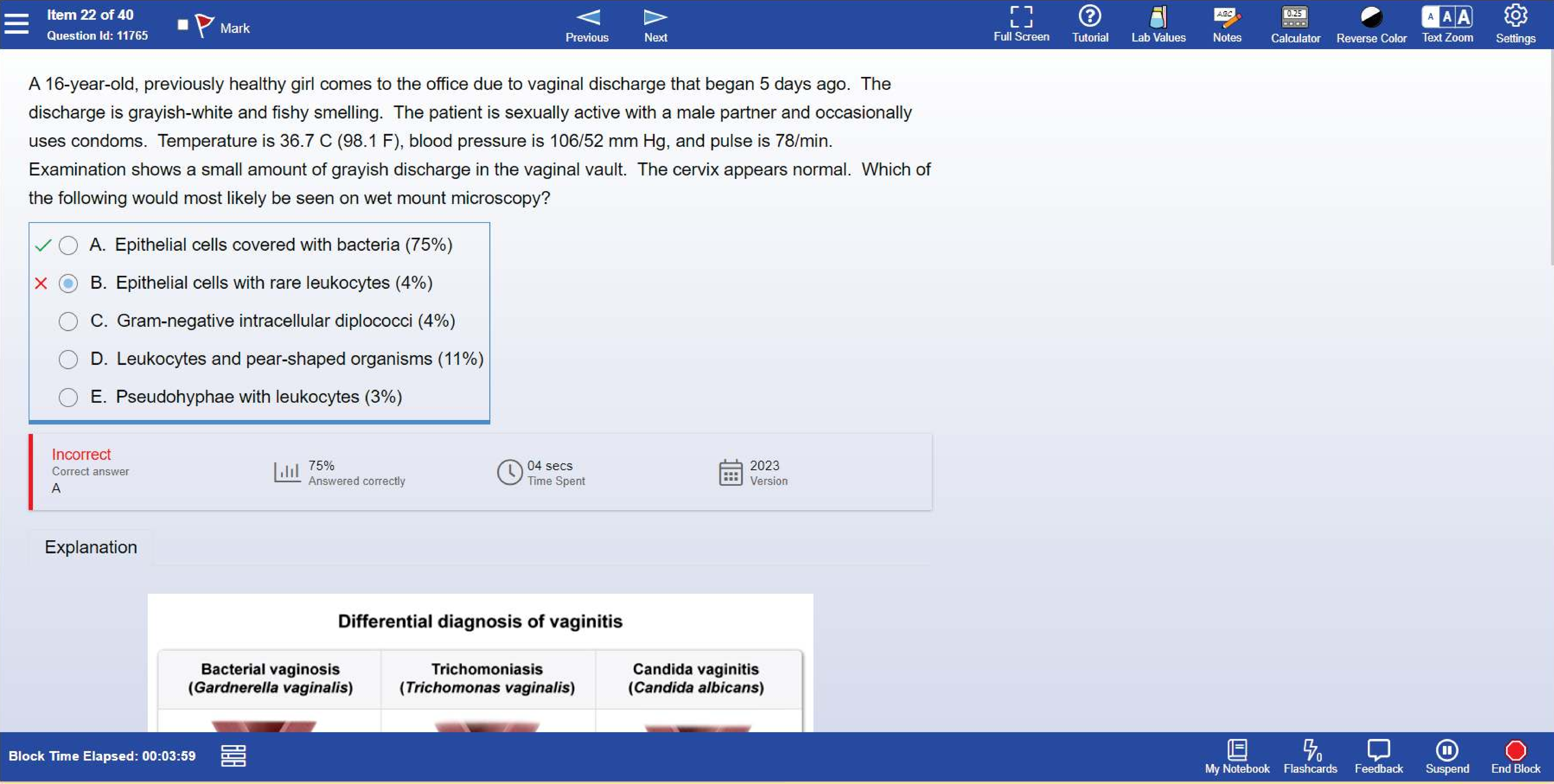
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A 16-year-old, previously healthy girl comes to the office due to vaginal discharge that began 5 days ago. The discharge is grayish-white and fishy smelling. The patient is sexually active with a male partner and occasionally uses condoms. Temperature is 36.7 C (98.1 F), blood pressure is 106/52 mm Hg, and pulse is 78/min. Examination shows a small amount of grayish discharge in the vaginal vault. The cervix appears normal. Which of the following would most likely be seen on wet mount microscopy?

- ✓ ○ A. Epithelial cells covered with bacteria (75%)
- ✗ ● B. Epithelial cells with rare leukocytes (4%)
- ○ C. Gram-negative intracellular diplococci (4%)
- ○ D. Leukocytes and pear-shaped organisms (11%)
- ○ E. Pseudohyphae with leukocytes (3%)

Incorrect
Correct answer
A

75%
Answered correctly

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Explanation

Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	**Trichomoniasis (*Trichomonas vaginalis*)**	**Candida vaginitis (*Candida albicans*)**

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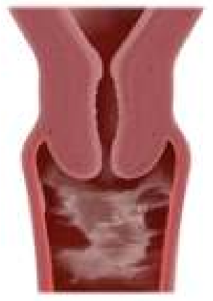
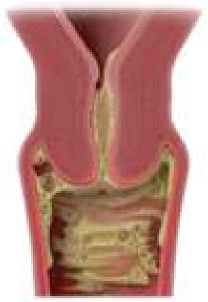
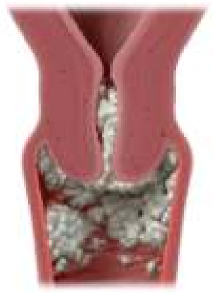
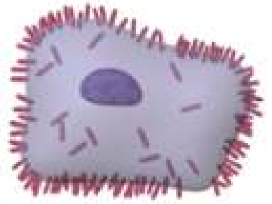
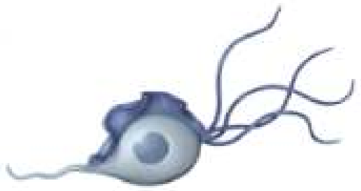
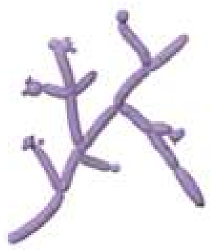
Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	Trichomoniasis (*Trichomonas vaginalis*)	Candida vaginitis (*Candida albicans*)
 • Thin, off-white discharge with fishy odor • No inflammation	 • Thin, yellow-green, malodorous, frothy discharge • Vaginal inflammation	 • Thick, cottage cheese discharge • Vaginal inflammation
 • pH >4.5 • Clue cells • Positive whiff test (amine odor with KOH)	 • pH >4.5 • Motile trichomonads	 • Normal pH (3.8-4.5) • Pseudohyphae
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

KOH = potassium hydroxide.

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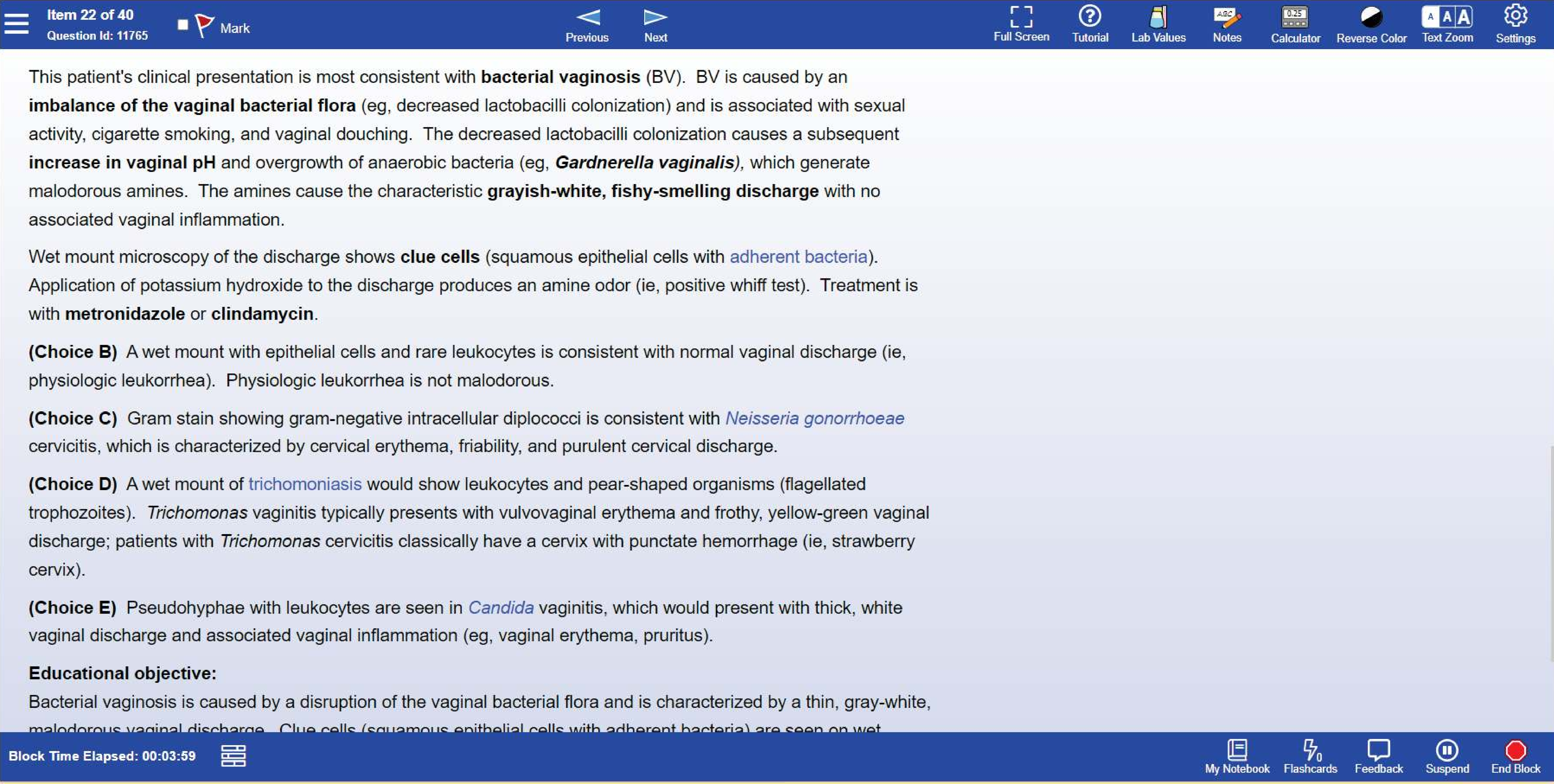


This patient's clinical presentation is most consistent with **bacterial vaginosis** (BV). BV is caused by an **imbalance of the vaginal bacterial flora** (eg, decreased lactobacilli colonization) and is associated with sexual activity, cigarette smoking, and vaginal douching. The decreased lactobacilli colonization causes a subsequent **increase in vaginal pH** and overgrowth of anaerobic bacteria (eg, ***Gardnerella vaginalis***), which generate malodorous amines. The amines cause the characteristic **grayish-white, fishy-smelling discharge** with no associated vaginal inflammation.

Wet mount microscopy of the discharge shows **clue cells** (squamous epithelial cells with adherent bacteria). Application of potassium hydroxide to the discharge produces an amine odor (ie, positive whiff test). Treatment is with **metronidazole** or **clindamycin**.

(Choice B) A wet mount with epithelial cells and rare leukocytes is consistent with normal vaginal discharge (ie, physiologic leukorrhea). Physiologic leukorrhea is not malodorous.

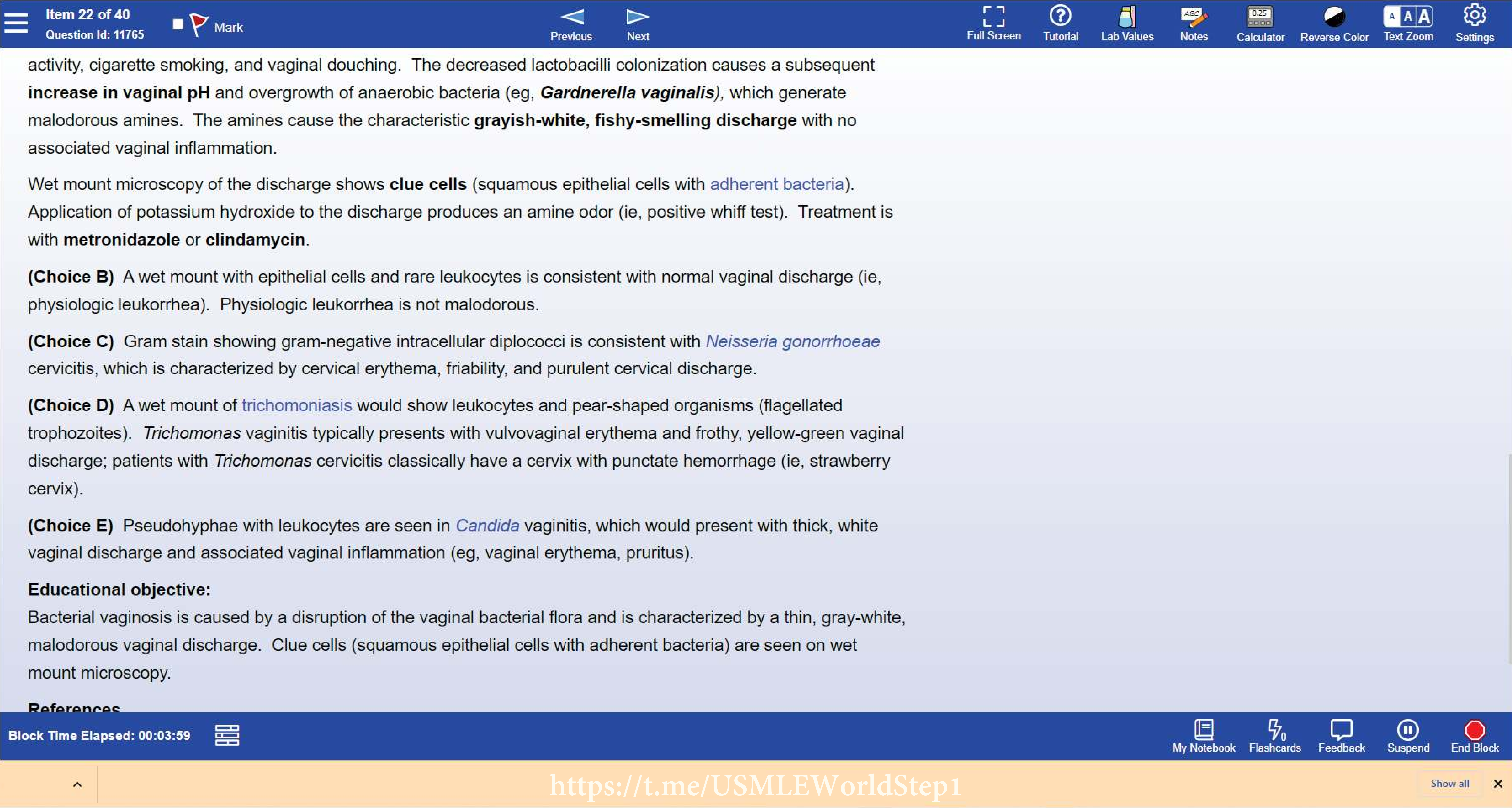
(Choice C) Gram stain showing gram-negative intracellular diplococci is consistent with *Neisseria gonorrhoeae* cervicitis, which is characterized by cervical erythema, friability, and purulent cervical discharge.

(Choice D) A wet mount of trichomoniasis would show leukocytes and pear-shaped organisms (flagellated trophozoites). *Trichomonas* vaginitis typically presents with vulvovaginal erythema and frothy, yellow-green vaginal discharge; patients with *Trichomonas* cervicitis classically have a cervix with punctate hemorrhage (ie, strawberry cervix).

(Choice E) Pseudohyphae with leukocytes are seen in *Candida* vaginitis, which would present with thick, white vaginal discharge and associated vaginal inflammation (eg, vaginal erythema, pruritus).

Educational objective:

Bacterial vaginosis is caused by a disruption of the vaginal bacterial flora and is characterized by a thin, gray-white, malodorous vaginal discharge. Clue cells (squamous epithelial cells with adherent bacteria) are seen on wet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activity, cigarette smoking, and vaginal douching. The decreased lactobacilli colonization causes a subsequent **increase in vaginal pH** and overgrowth of anaerobic bacteria (eg, ***Gardnerella vaginalis***), which generate malodorous amines. The amines cause the characteristic **grayish-white, fishy-smelling discharge** with no associated vaginal inflammation.

Wet mount microscopy of the discharge shows **clue cells** (squamous epithelial cells with adherent bacteria). Application of potassium hydroxide to the discharge produces an amine odor (ie, positive whiff test). Treatment is with **metronidazole** or **clindamycin**.

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Educational objective:

Bacterial vaginosis is caused by a disruption of the vaginal bacterial flora and is characterized by a thin, gray-white, malodorous vaginal discharge. Clue cells (squamous epithelial cells with adherent bacteria) are seen on wet mount microscopy.

References

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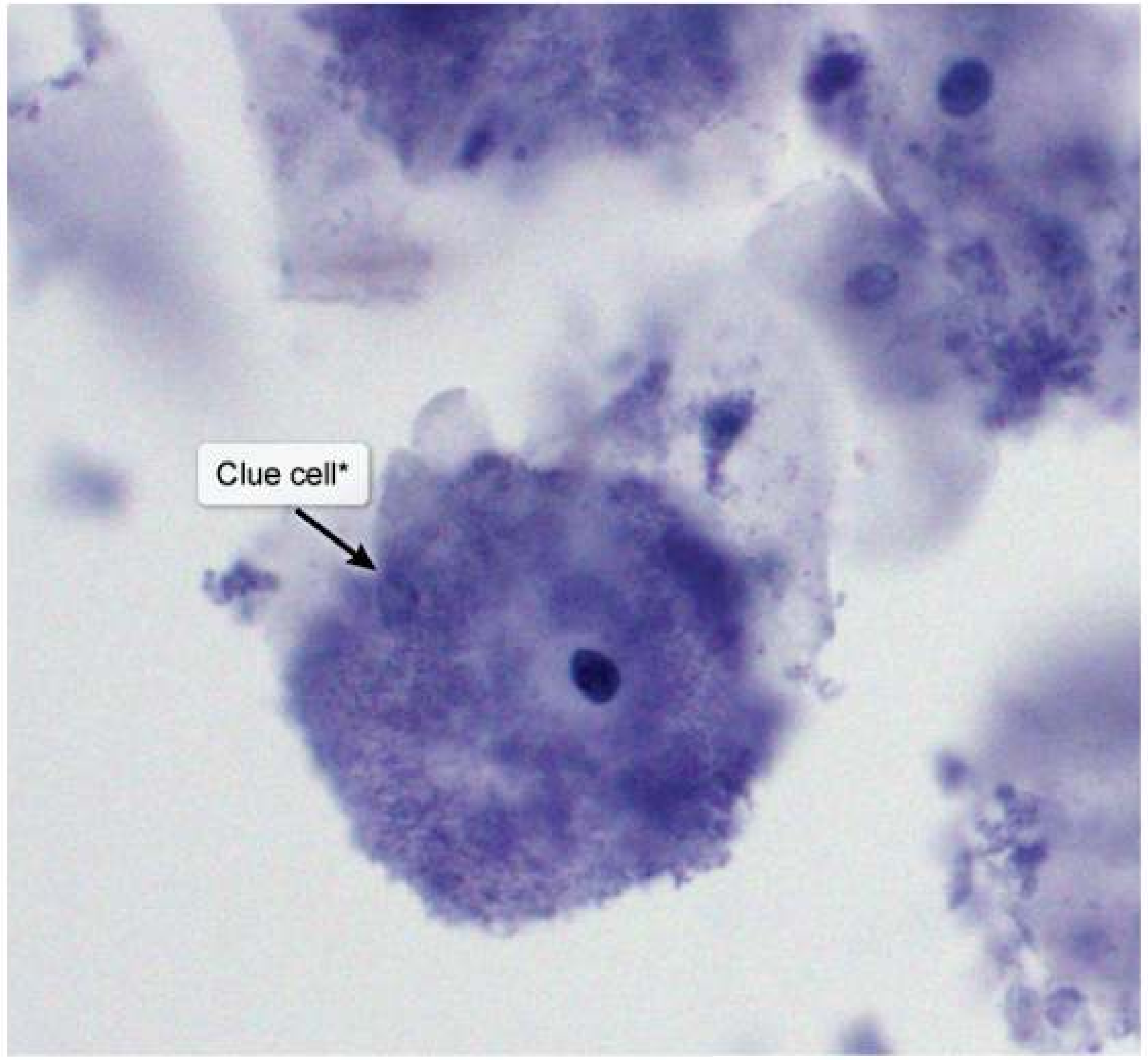
Bacterial vaginosis



*Squamous cell with adherent bacteria (eg, *Gardnerella*)

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(Choice E) Pseudohyphae with leukocytes are seen in *Candida* vaginitis, which would present with thick, white

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KOH = potassium hydroxide. ©UWorld

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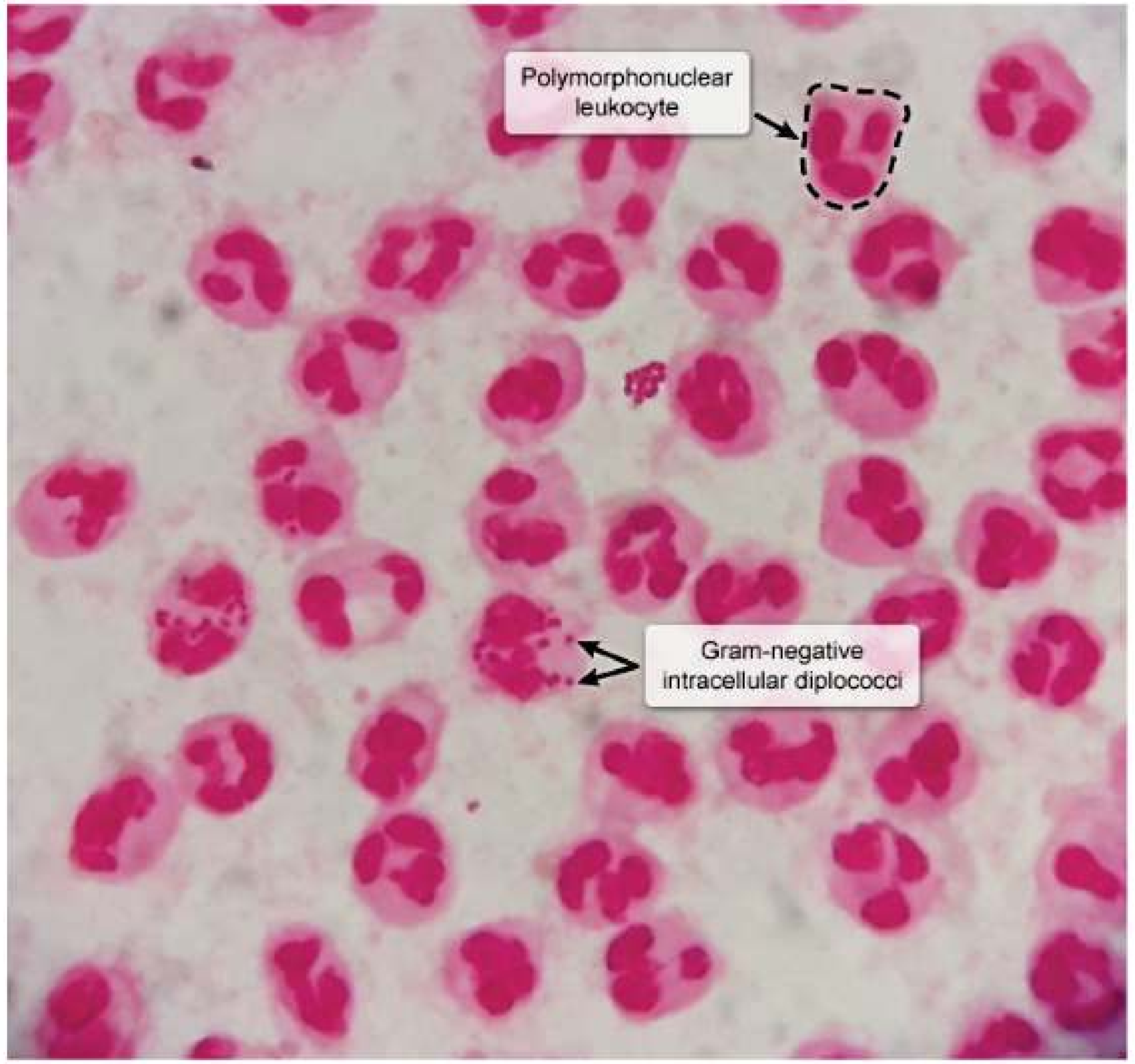
Neisseria gonorrhoeae


Polymorphonuclear leukocyte
Gram-negative intracellular diplococci

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KOH = potassium hydroxide. ©UWorld

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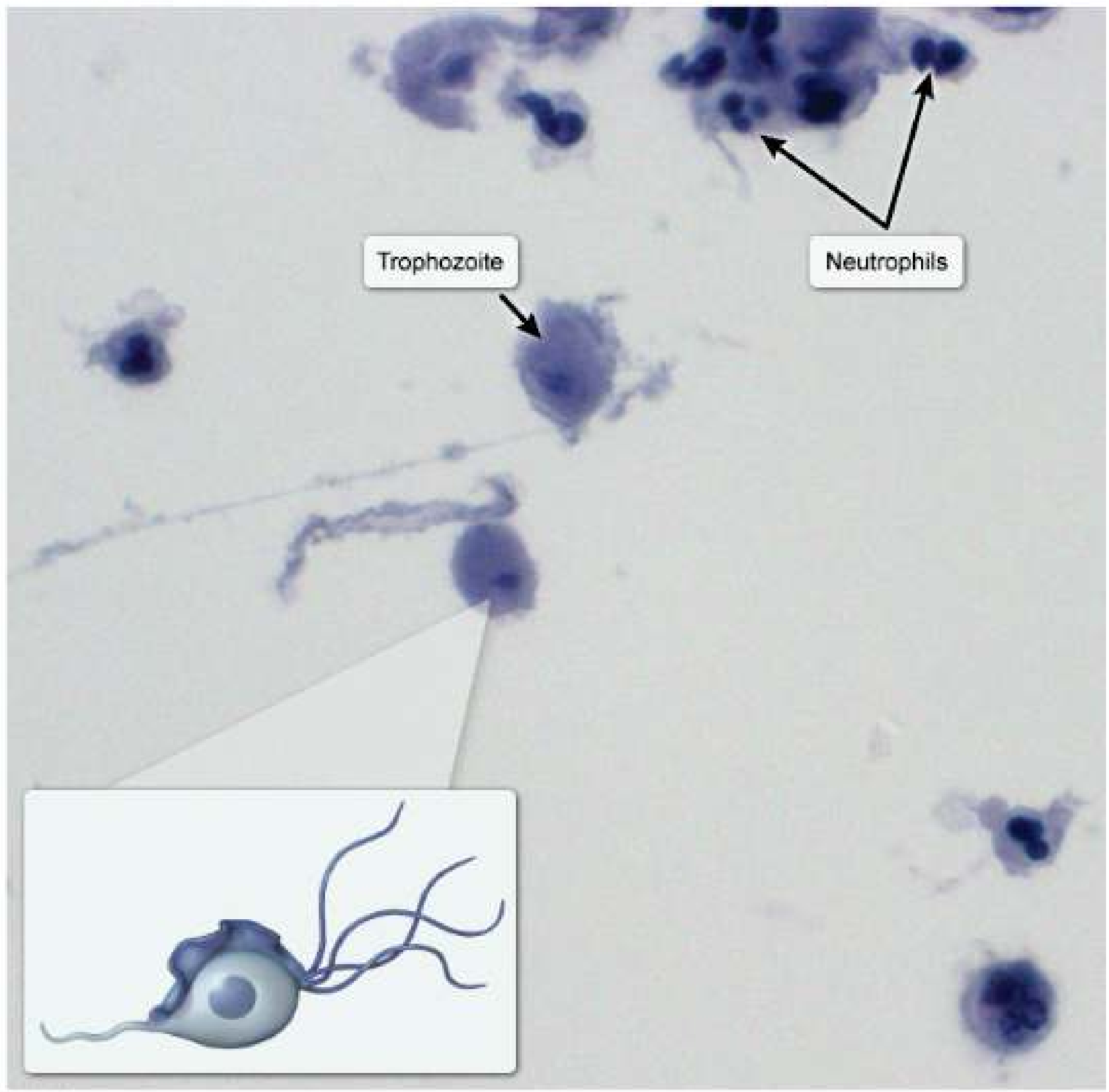
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Neutrophils

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Bacterial vaginosis is caused by a disruption of the vaginal bacterial flora and is characterized by a thin, gray-white,

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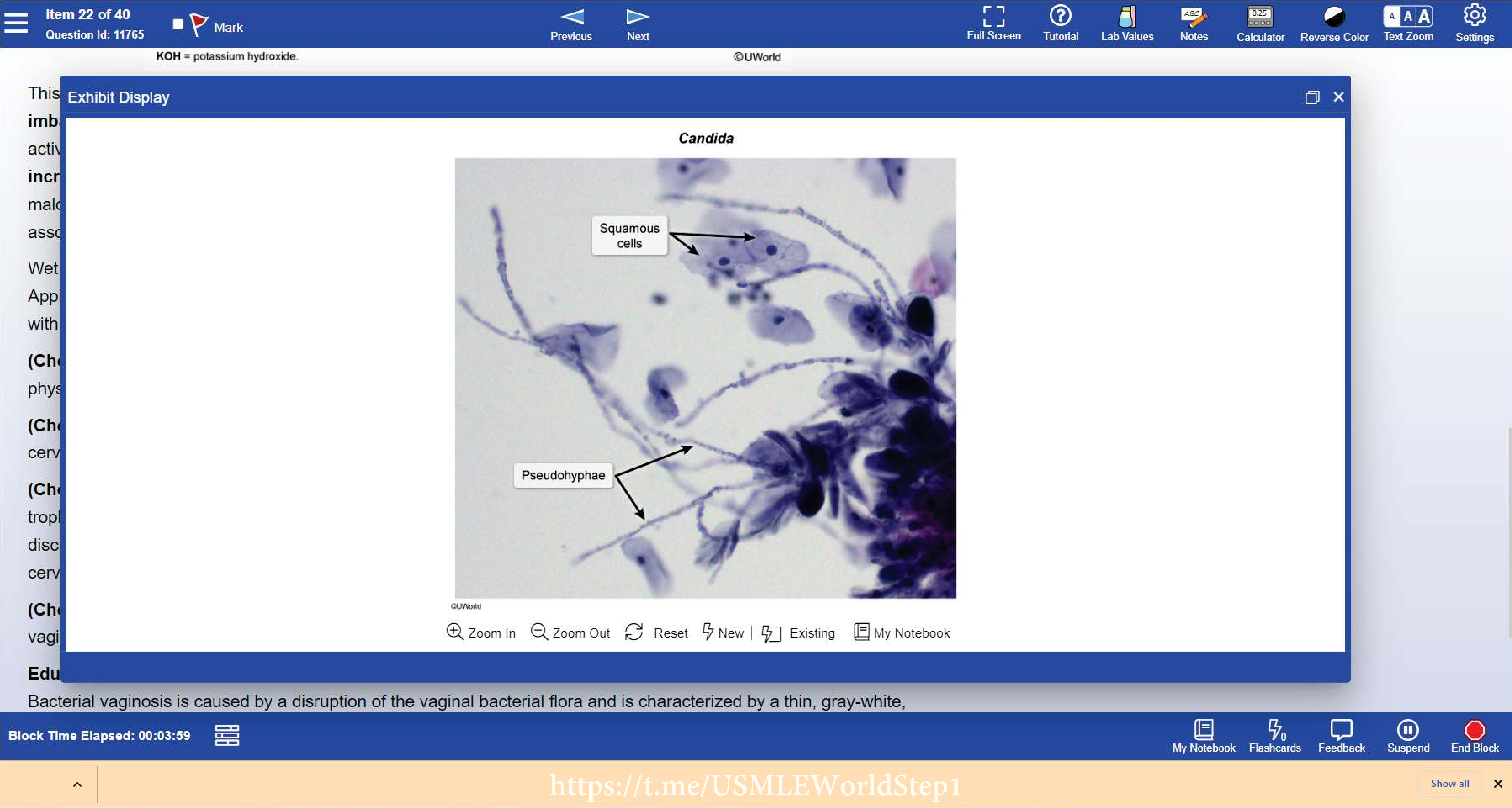
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KOH = potassium hydroxide.

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Bacterial vaginosis is caused by a disruption of the vaginal bacterial flora and is characterized by a thin, gray-white,

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Candida

Squamous cells
Pseudohyphae
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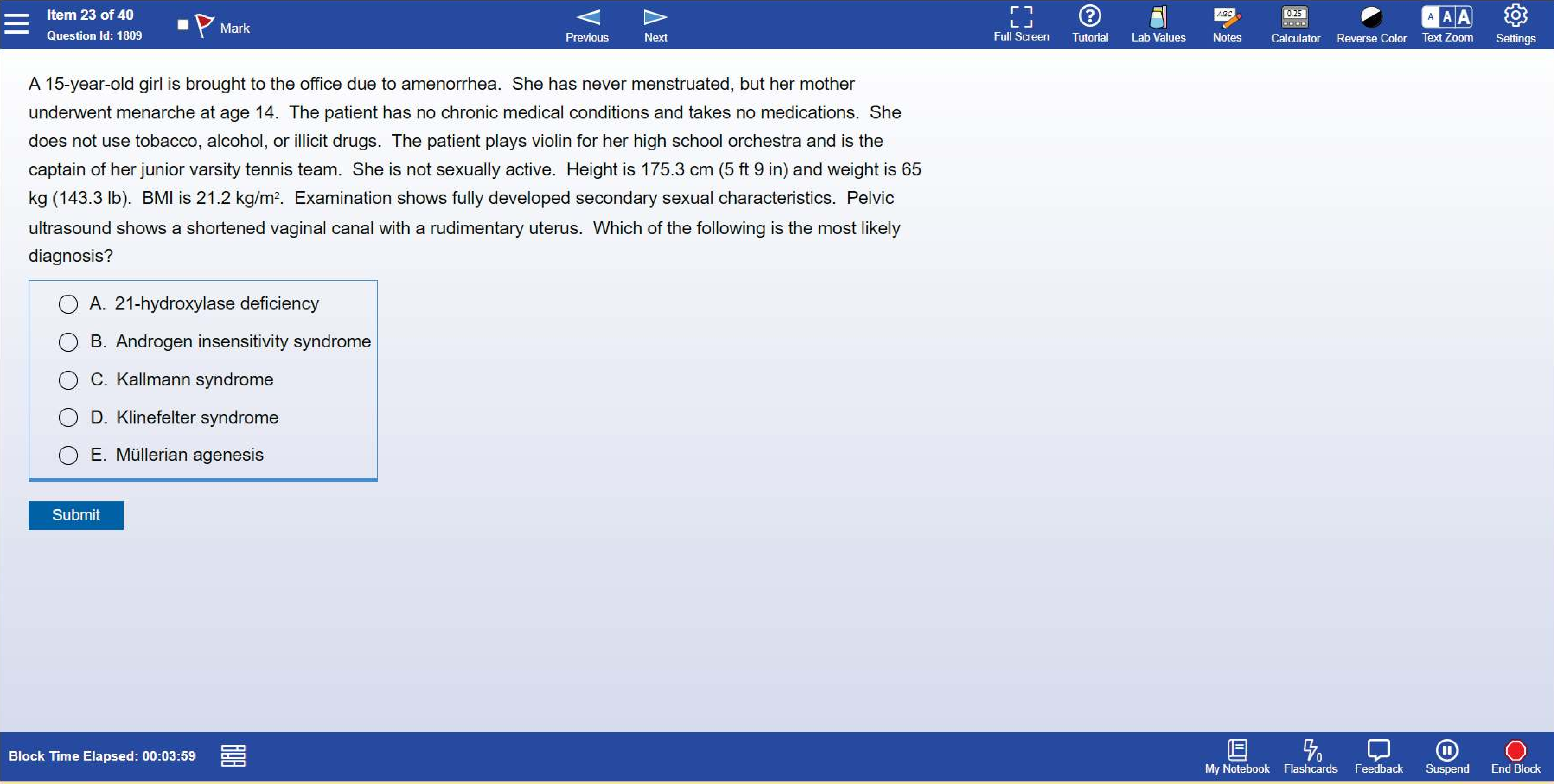
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A 15-year-old girl is brought to the office due to amenorrhea. She has never menstruated, but her mother underwent menarche at age 14. The patient has no chronic medical conditions and takes no medications. She does not use tobacco, alcohol, or illicit drugs. The patient plays violin for her high school orchestra and is the captain of her junior varsity tennis team. She is not sexually active. Height is 175.3 cm (5 ft 9 in) and weight is 65 kg (143.3 lb). BMI is 21.2 kg/m². Examination shows fully developed secondary sexual characteristics. Pelvic ultrasound shows a shortened vaginal canal with a rudimentary uterus. Which of the following is the most likely diagnosis?

- ○ A. 21-hydroxylase deficiency
- ○ B. Androgen insensitivity syndrome
- ○ C. Kallmann syndrome
- ○ D. Klinefelter syndrome
- ○ E. Müllerian agenesis

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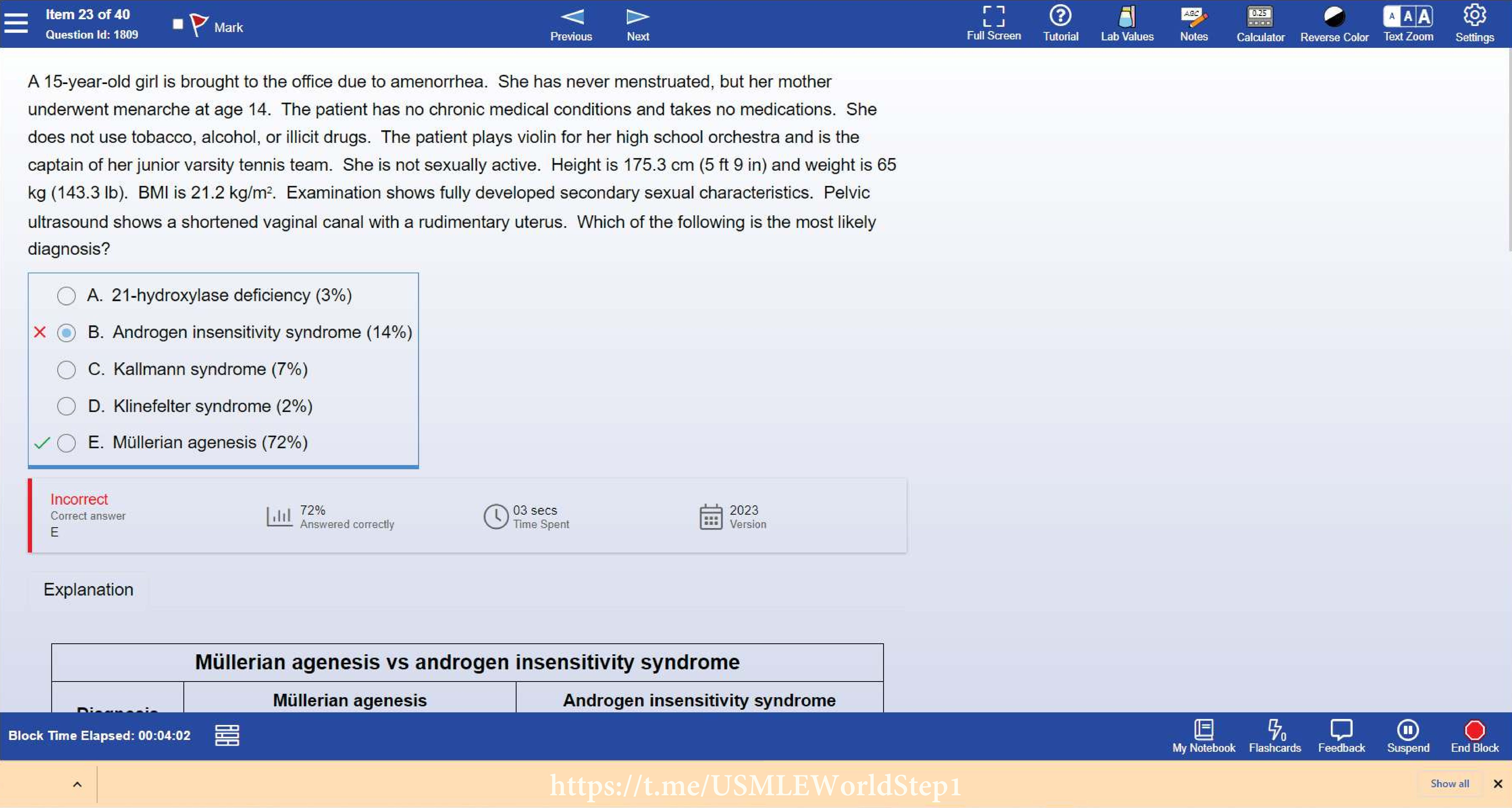
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○ A. 21-hydroxylase deficiency (3%)

✗ ● B. Androgen insensitivity syndrome (14%)

○ C. Kallmann syndrome (7%)

○ D. Klinefelter syndrome (2%)

✓ ○ E. Müllerian agenesis (72%)

Incorrect
Correct answer
E

72%
Answered correctly

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Explanation

Müllerian agenesis vs androgen insensitivity syndrome		
Diagnosis	Müllerian agenesis	Androgen insensitivity syndrome

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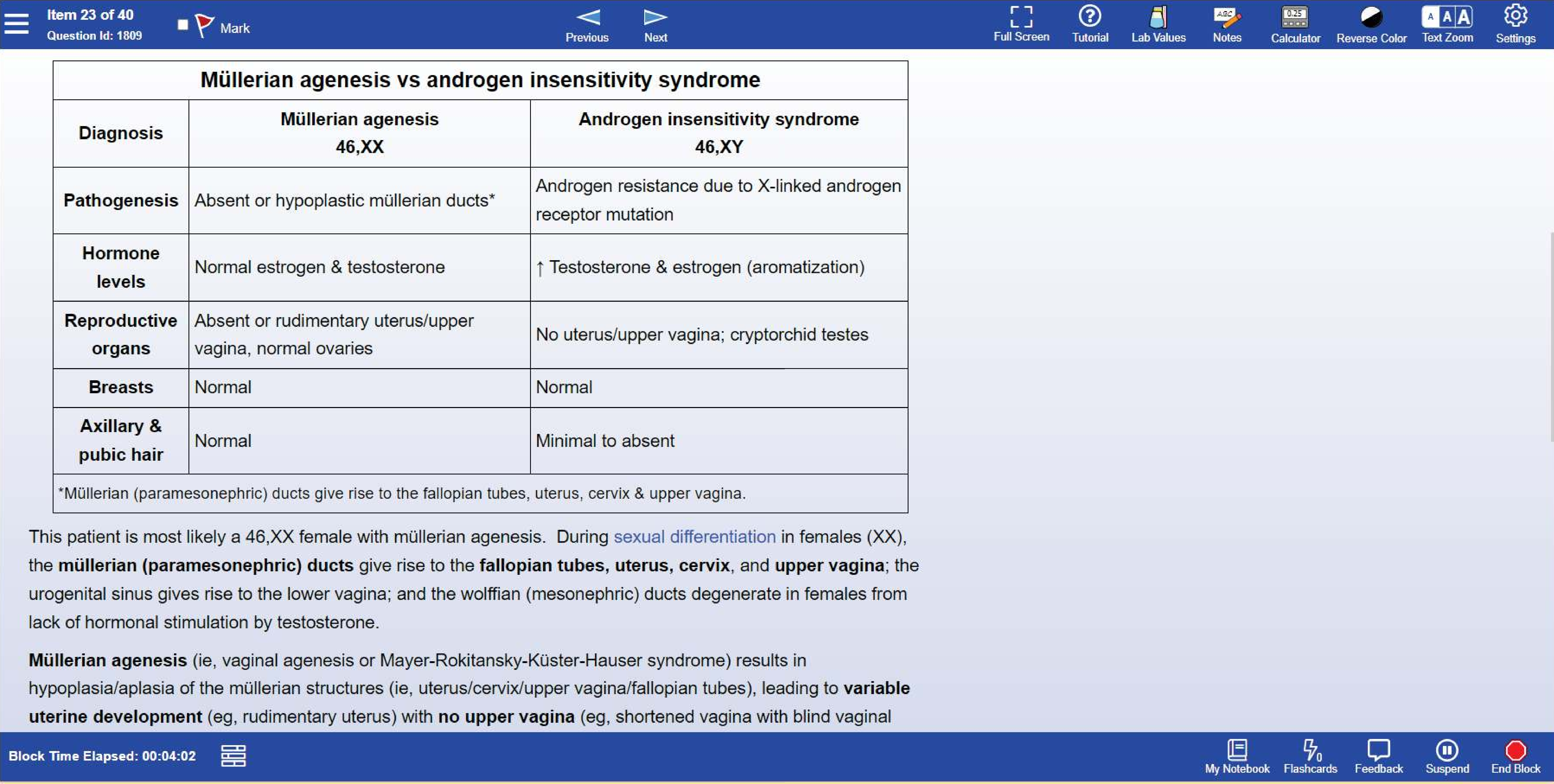
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Müllerian agenesis vs androgen insensitivity syndrome

Diagnosis	**Müllerian agenesis** **46,XX**	**Androgen insensitivity syndrome** **46,XY**
Pathogenesis	Absent or hypoplastic müllerian ducts*	Androgen resistance due to X-linked androgen receptor mutation
Hormone levels	Normal estrogen & testosterone	↑ Testosterone & estrogen (aromatization)
Reproductive organs	Absent or rudimentary uterus/upper vagina, normal ovaries	No uterus/upper vagina; cryptorchid testes
Breasts	Normal	Normal
Axillary & pubic hair	Normal	Minimal to absent

*Müllerian (paramesonephric) ducts give rise to the fallopian tubes, uterus, cervix & upper vagina.

This patient is most likely a 46,XX female with müllerian agenesis. During sexual differentiation in females (XX), the **müllerian (paramesonephric) ducts** give rise to the **fallopian tubes, uterus, cervix**, and **upper vagina**; the urogenital sinus gives rise to the lower vagina; and the wolffian (mesonephric) ducts degenerate in females from lack of hormonal stimulation by testosterone.

Müllerian agenesis (ie, vaginal agenesis or Mayer-Rokitansky-Küster-Hauser syndrome) results in hypoplasia/aplasia of the müllerian structures (ie, uterus/cervix/upper vagina/fallopian tubes), leading to **variable uterine development** (eg, rudimentary uterus) with **no upper vagina** (eg, shortened vagina with blind vaginal

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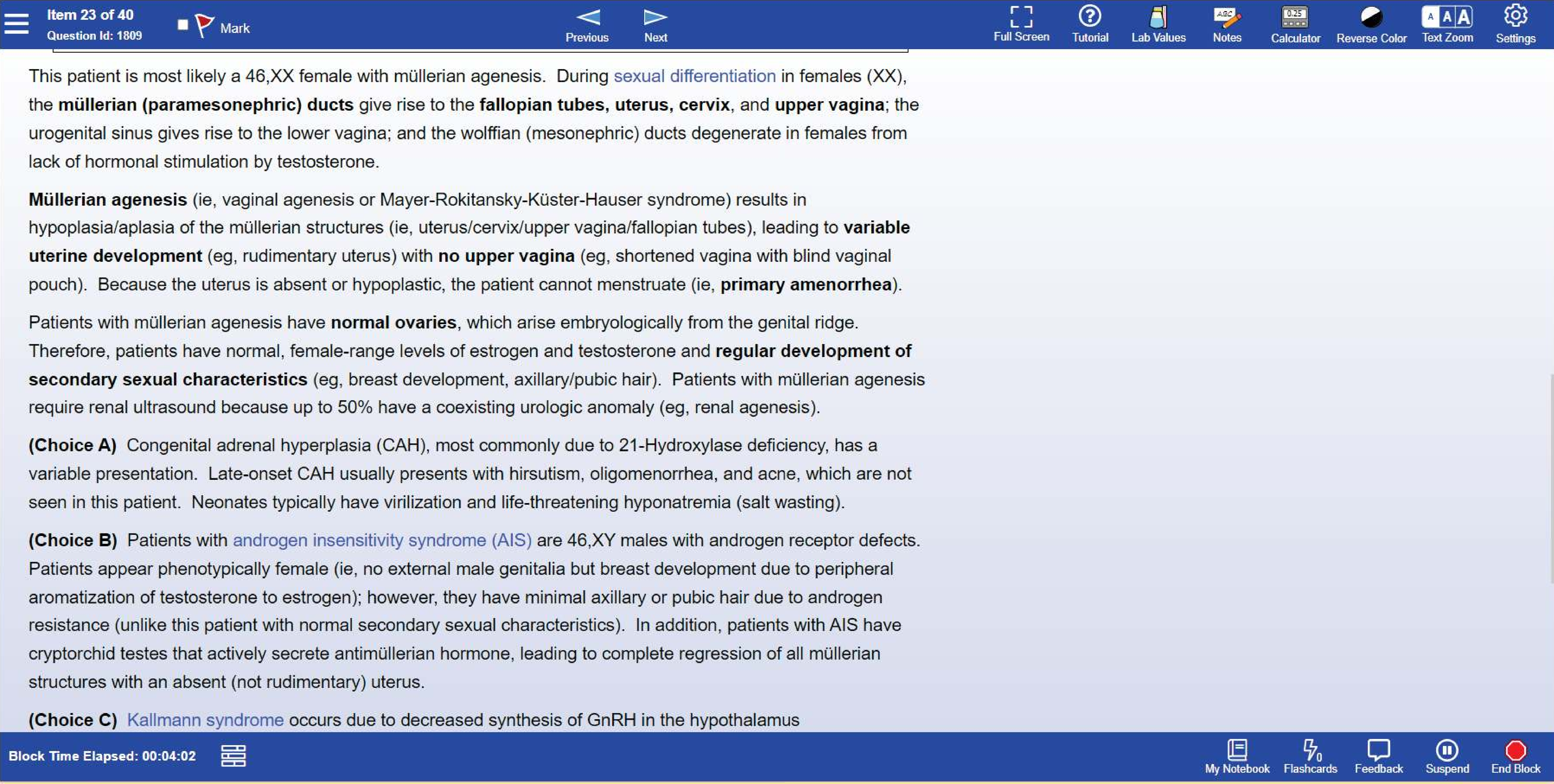

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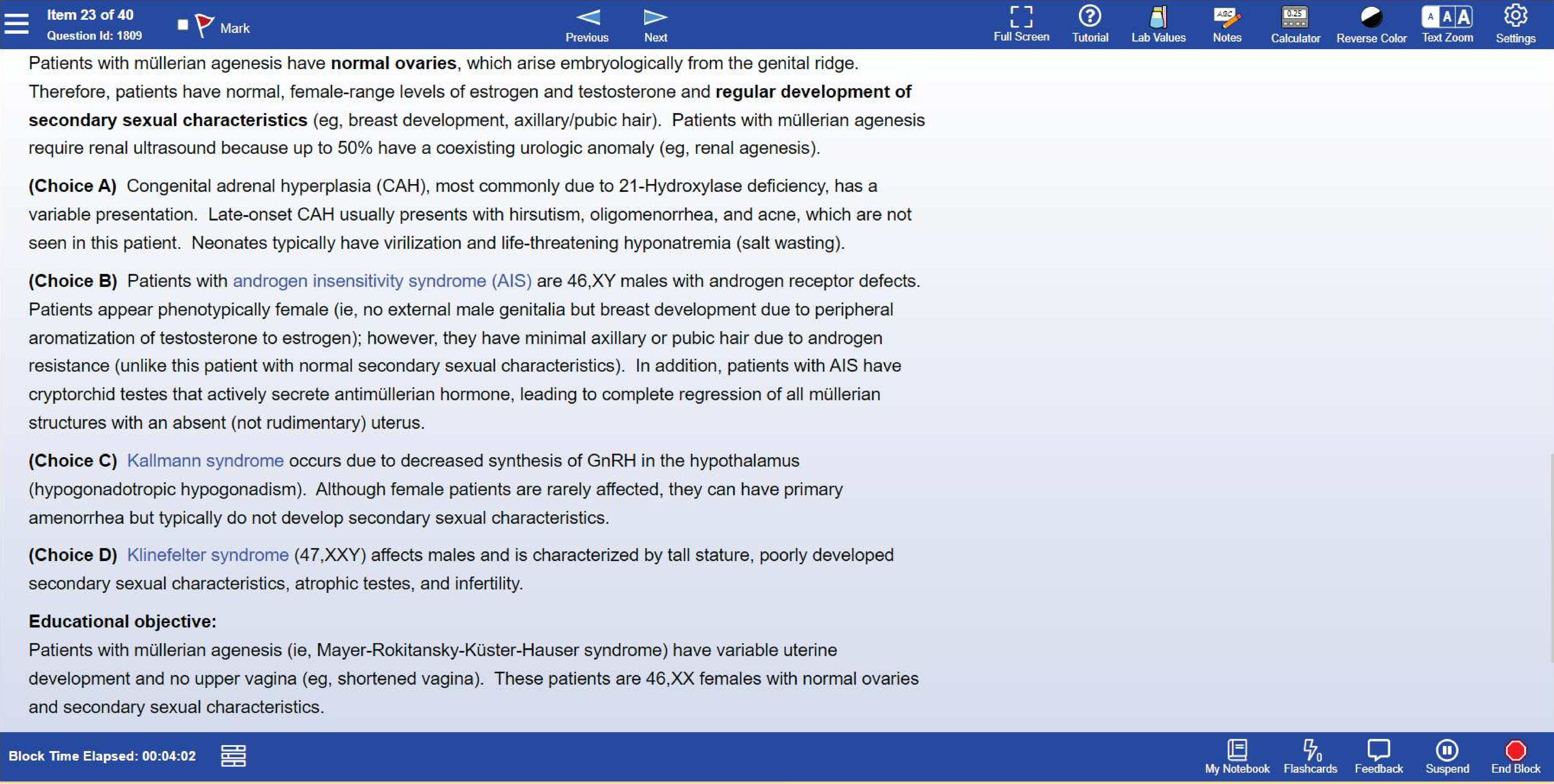
Müllerian agenesis (ie, vaginal agenesis or Mayer-Rokitansky-Küster-Hauser syndrome) results in hypoplasia/aplasia of the müllerian structures (ie, uterus/cervix/upper vagina/fallopian tubes), leading to **variable uterine development** (eg, rudimentary uterus) with **no upper vagina** (eg, shortened vagina with blind vaginal pouch). Because the uterus is absent or hypoplastic, the patient cannot menstruate (ie, **primary amenorrhea**).

Patients with müllerian agenesis have **normal ovaries**, which arise embryologically from the genital ridge. Therefore, patients have normal, female-range levels of estrogen and testosterone and **regular development of secondary sexual characteristics** (eg, breast development, axillary/pubic hair). Patients with müllerian agenesis require renal ultrasound because up to 50% have a coexisting urologic anomaly (eg, renal agenesis).

(Choice A) Congenital adrenal hyperplasia (CAH), most commonly due to 21-Hydroxylase deficiency, has a variable presentation. Late-onset CAH usually presents with hirsutism, oligomenorrhea, and acne, which are not seen in this patient. Neonates typically have virilization and life-threatening hyponatremia (salt wasting).

(Choice B) Patients with androgen insensitivity syndrome (AIS) are 46,XY males with androgen receptor defects. Patients appear phenotypically female (ie, no external male genitalia but breast development due to peripheral aromatization of testosterone to estrogen); however, they have minimal axillary or pubic hair due to androgen resistance (unlike this patient with normal secondary sexual characteristics). In addition, patients with AIS have cryptorchid testes that actively secrete antimüllerian hormone, leading to complete regression of all müllerian structures with an absent (not rudimentary) uterus.

(Choice C) Kallmann syndrome occurs due to decreased synthesis of GnRH in the hypothalamus



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(Choice A) Congenital adrenal hyperplasia (CAH), most commonly due to 21-Hydroxylase deficiency, has a variable presentation. Late-onset CAH usually presents with hirsutism, oligomenorrhea, and acne, which are not seen in this patient. Neonates typically have virilization and life-threatening hyponatremia (salt wasting).

(Choice B) Patients with androgen insensitivity syndrome (AIS) are 46,XY males with androgen receptor defects. Patients appear phenotypically female (ie, no external male genitalia but breast development due to peripheral aromatization of testosterone to estrogen); however, they have minimal axillary or pubic hair due to androgen resistance (unlike this patient with normal secondary sexual characteristics). In addition, patients with AIS have cryptorchid testes that actively secrete antimüllerian hormone, leading to complete regression of all müllerian structures with an absent (not rudimentary) uterus.

(Choice C) Kallmann syndrome occurs due to decreased synthesis of GnRH in the hypothalamus (hypogonadotropic hypogonadism). Although female patients are rarely affected, they can have primary amenorrhea but typically do not develop secondary sexual characteristics.

(Choice D) Klinefelter syndrome (47,XXY) affects males and is characterized by tall stature, poorly developed secondary sexual characteristics, atrophic testes, and infertility.

Educational objective:

Patients with müllerian agenesis (ie, Mayer-Rokitansky-Küster-Hauser syndrome) have variable uterine development and no upper vagina (eg, shortened vagina). These patients are 46,XX females with normal ovaries and secondary sexual characteristics.

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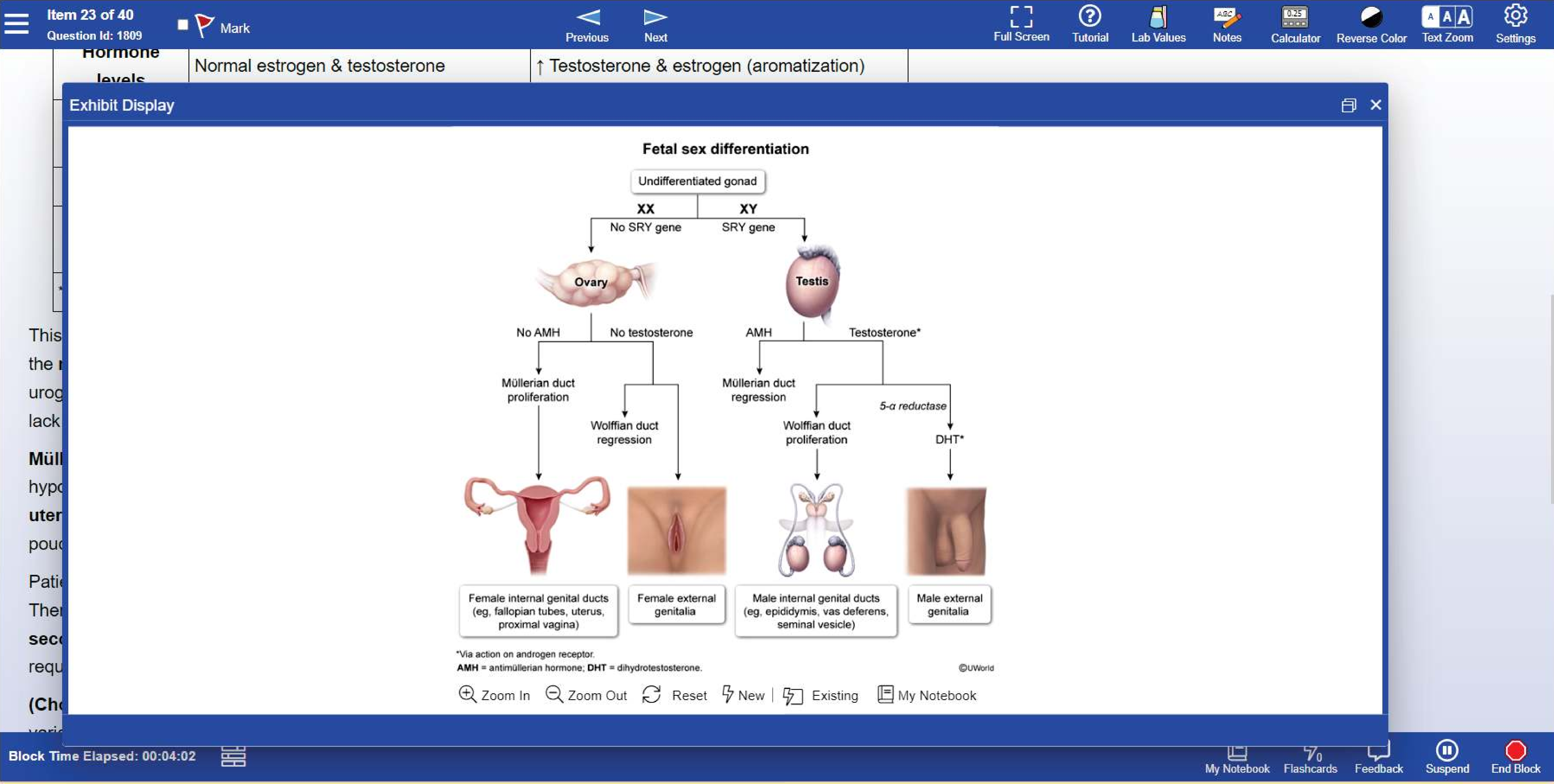
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Hormone levels	Normal estrogen & testosterone	↑ Testosterone & estrogen (aromatization)

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Fetal sex differentiation

Undifferentiated gonad
XX
No SRY gene
XY
SRY gene
Ovary
Testis
No AMH
No testosterone
AMH
Testosterone*
Müllerian duct proliferation
Wolffian duct regression
Müllerian duct regression
5-α reductase
Wolffian duct proliferation
DHT*
Female internal genital ducts (eg, fallopian tubes, uterus, proximal vagina)
Female external genitalia
Male internal genital ducts (eg, epididymis, vas deferens, seminal vesicle)
Male external genitalia

*Via action on androgen receptor.

AMH = antimüllerian hormone; **DHT** = dihydrotestosterone.

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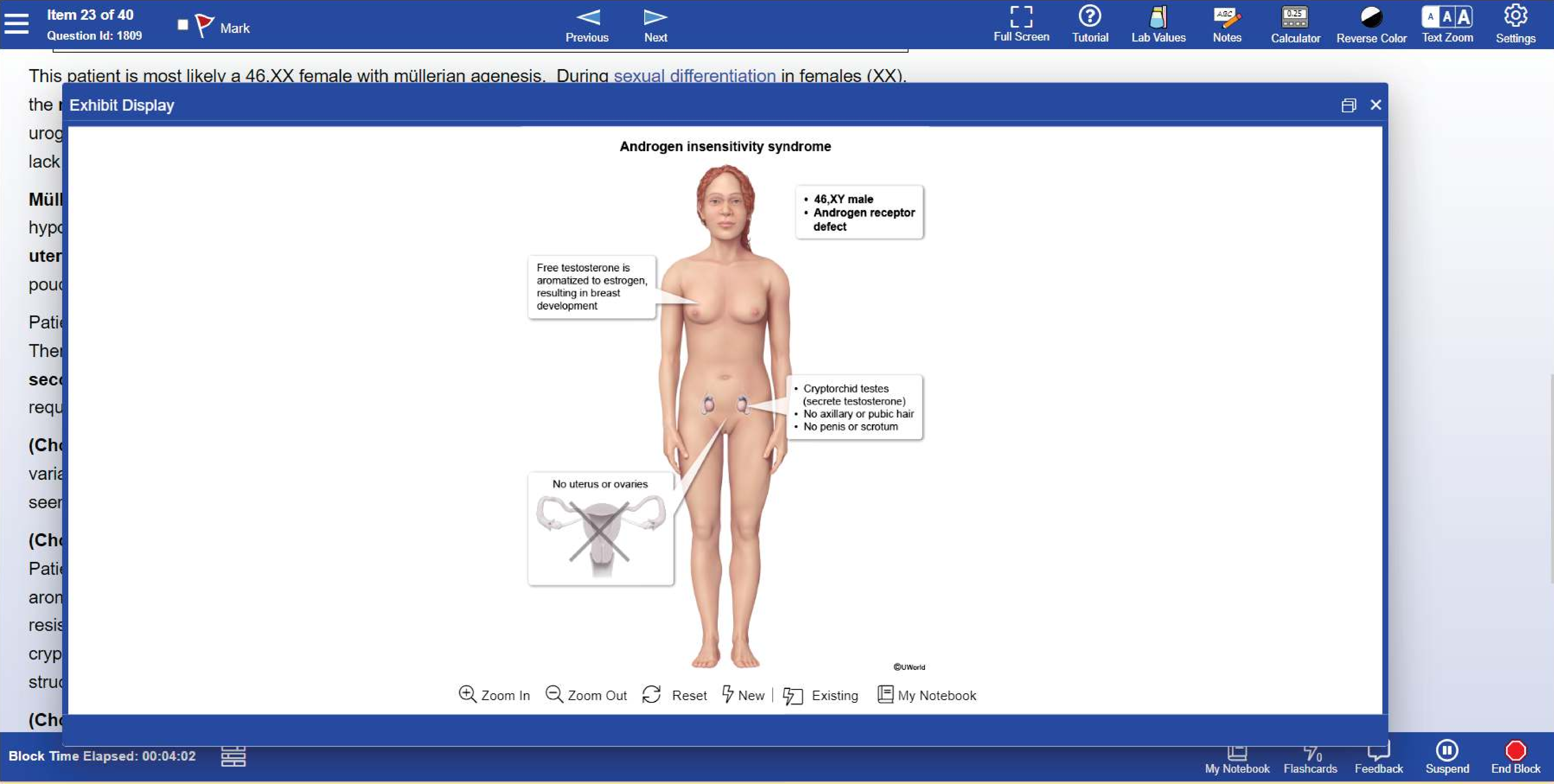

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This patient is most likely a 46,XX female with müllerian agenesis. During sexual differentiation in females (XX),

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Androgen insensitivity syndrome

- **46,XY male**
- **Androgen receptor defect**

Free testosterone is aromatized to estrogen, resulting in breast development

- Cryptorchid testes (secrete testosterone)
- No axillary or pubic hair
- No penis or scrotum

No uterus or ovaries

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Patients with müllerian agenesis have **normal ovaries**, which arise embryologically from the genital ridge.

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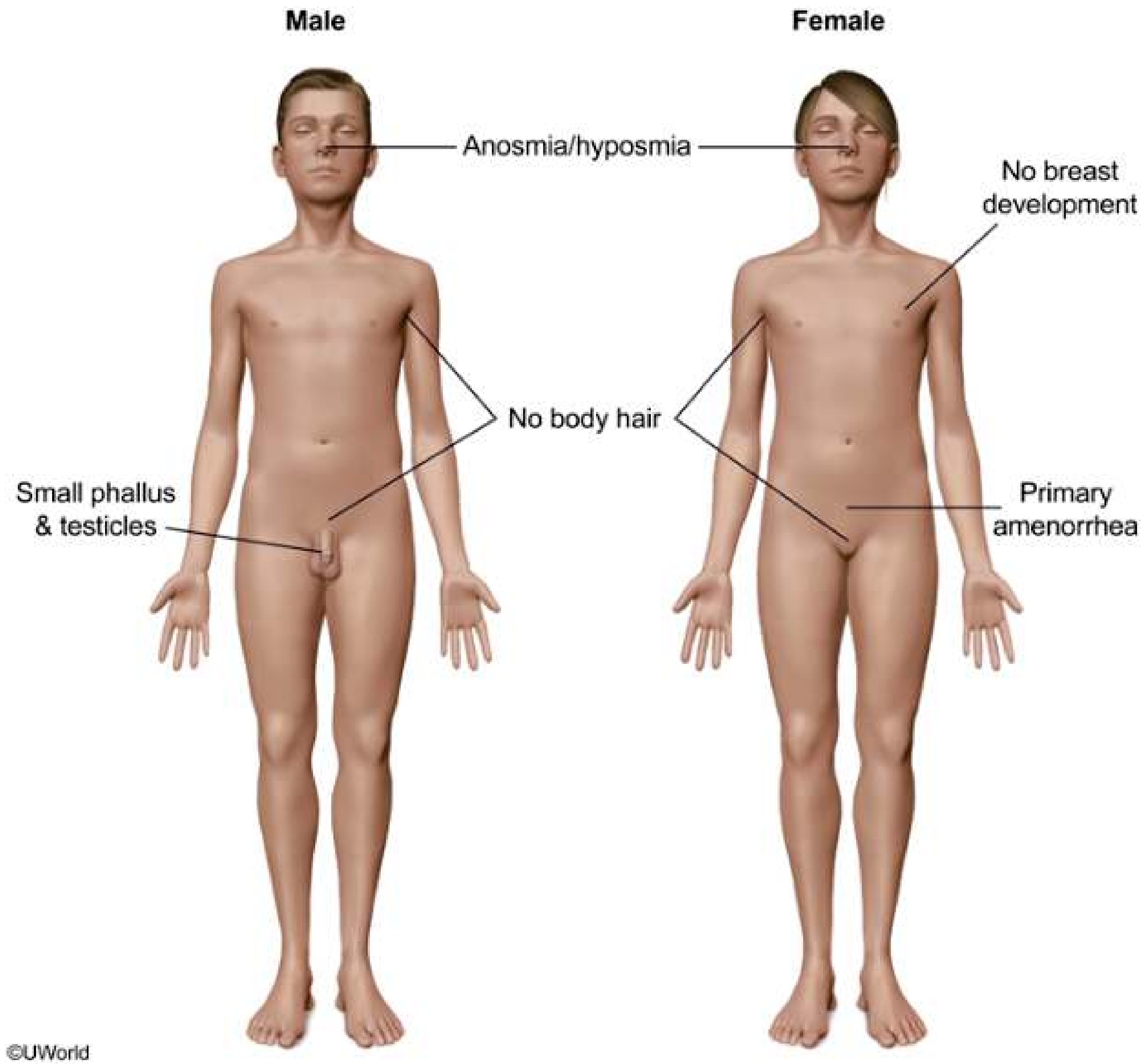
Kallmann syndrome


Male
Female
Anosmia/hyposmia
No breast development
No body hair
Small phallus & testicles
Primary amenorrhea
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Patients with müllerian agenesis have **normal ovaries**, which arise embryologically from the genital ridge.

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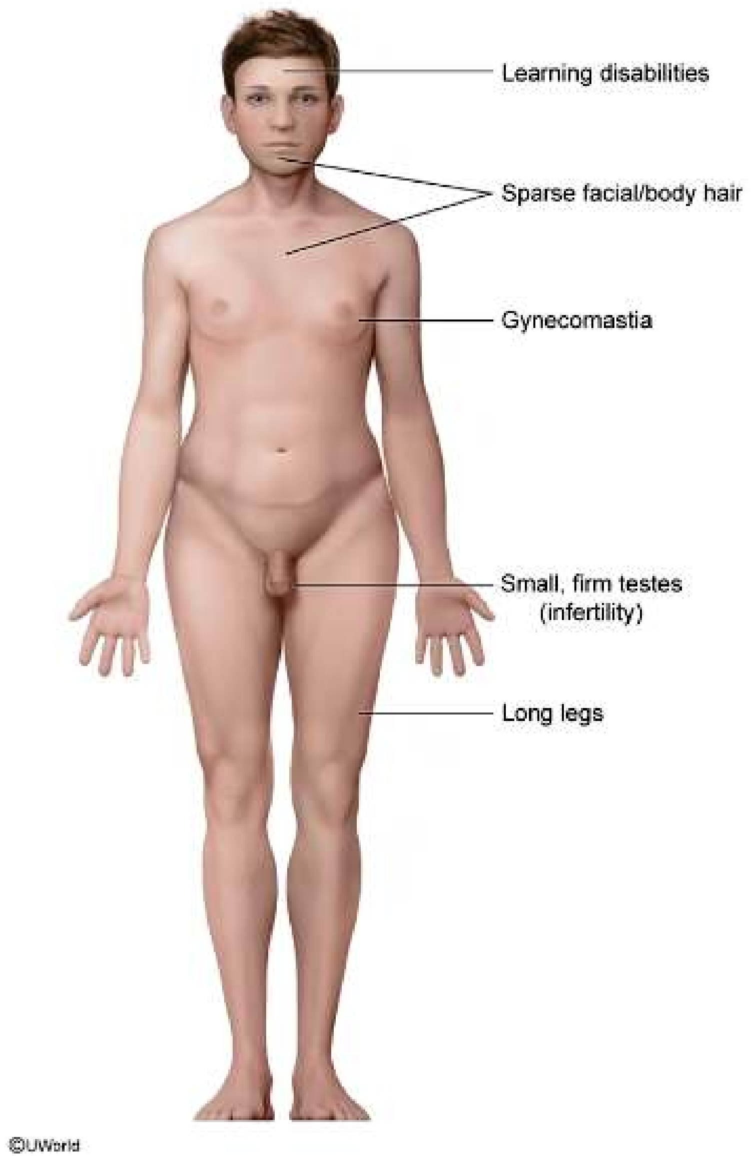
Klinefelter syndrome (47,XXY)


Learning disabilities
Sparse facial/body hair
Gynecomastia
Small, firm testes (infertility)
Long legs
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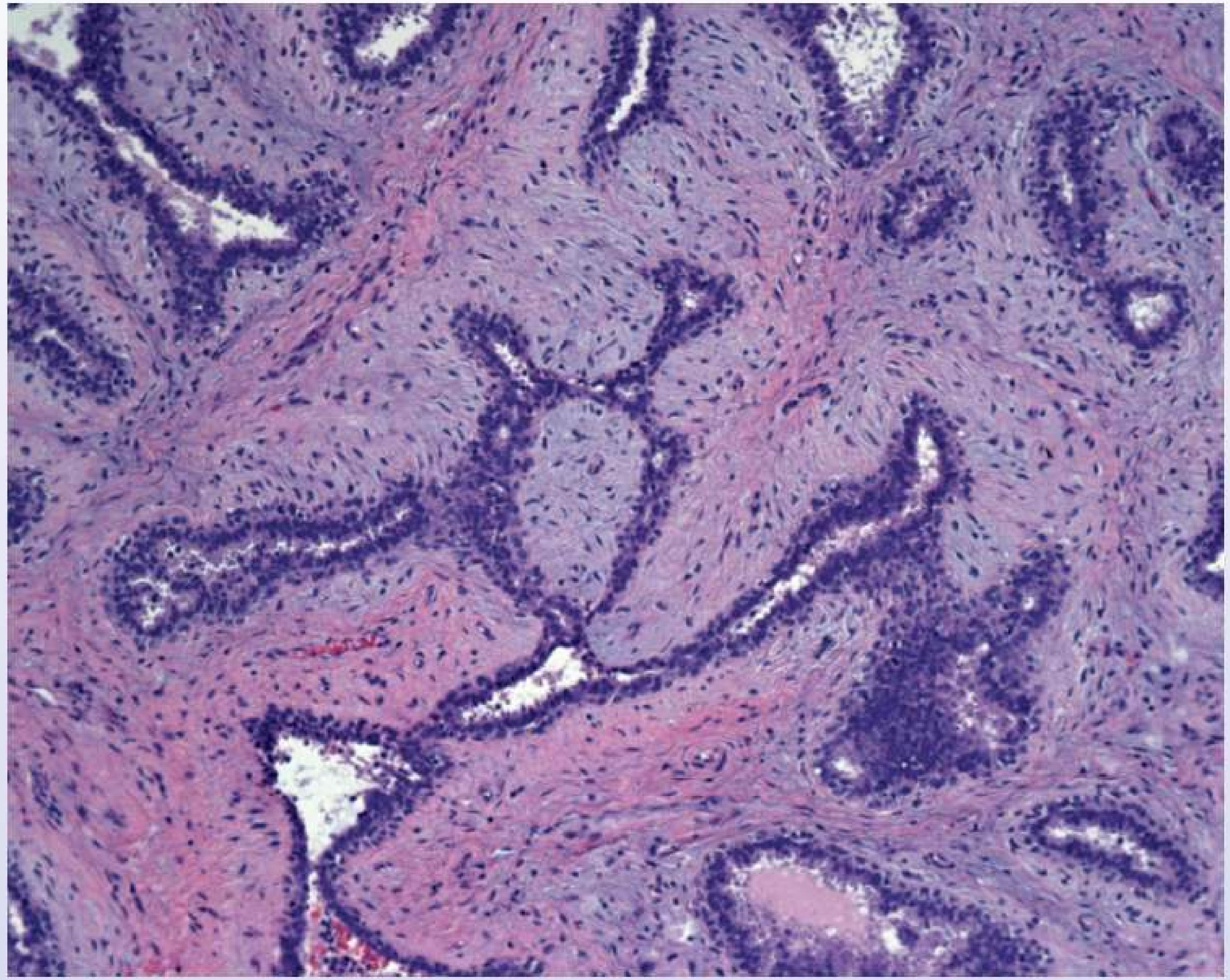
A 34-year-old woman comes to the clinic due to a mass in her right breast. The patient noticed the mass last week while in the shower. She has no chronic medical conditions and takes no daily medications. A 2-cm nodule is noted on examination of the right breast, and the patient is referred for biopsy. Histologic evaluation of the tissue specimen is shown in the image below:



Which of the following is the most likely diagnosis?

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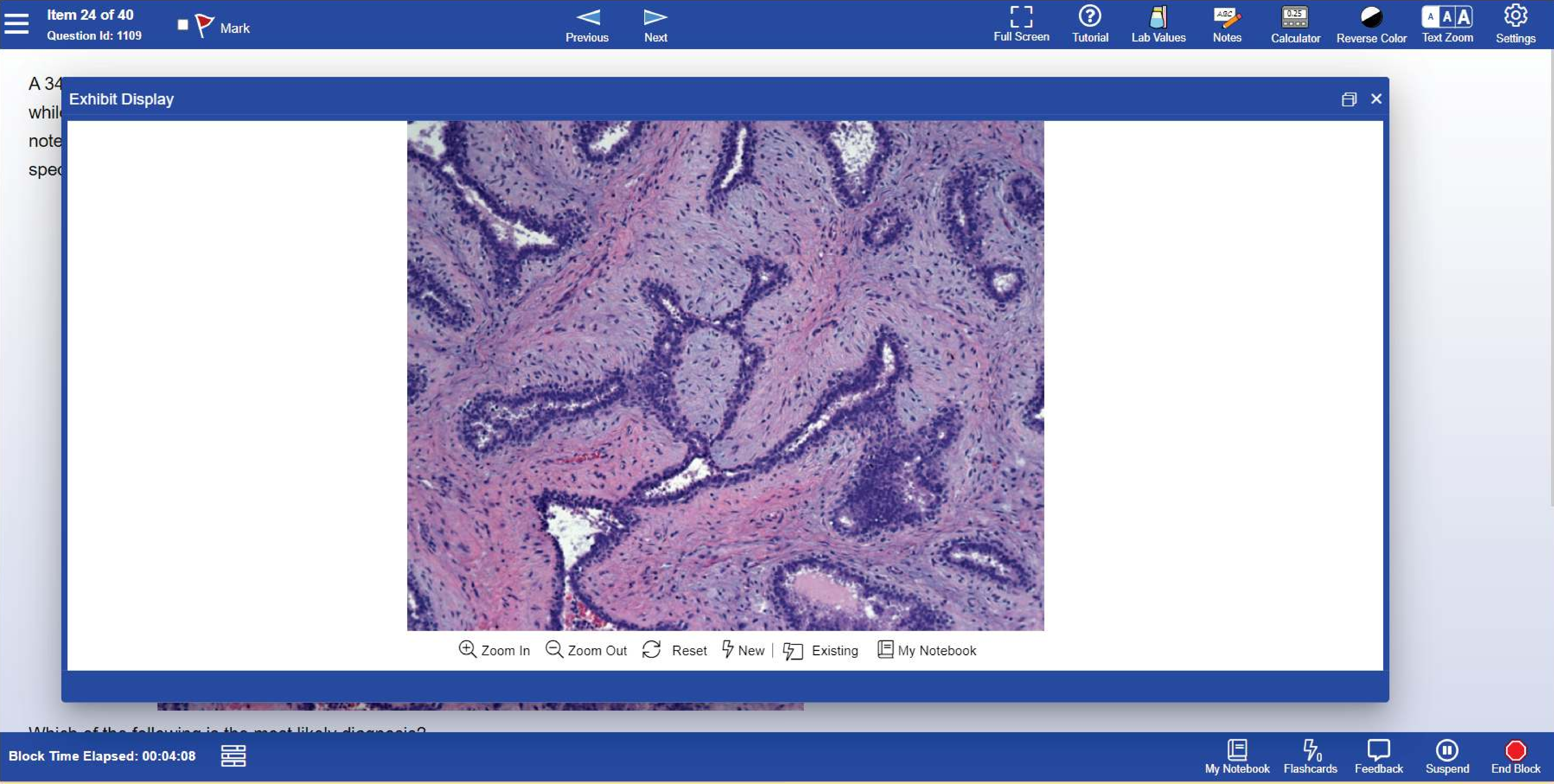
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Which of the following is the most likely diagnosis?

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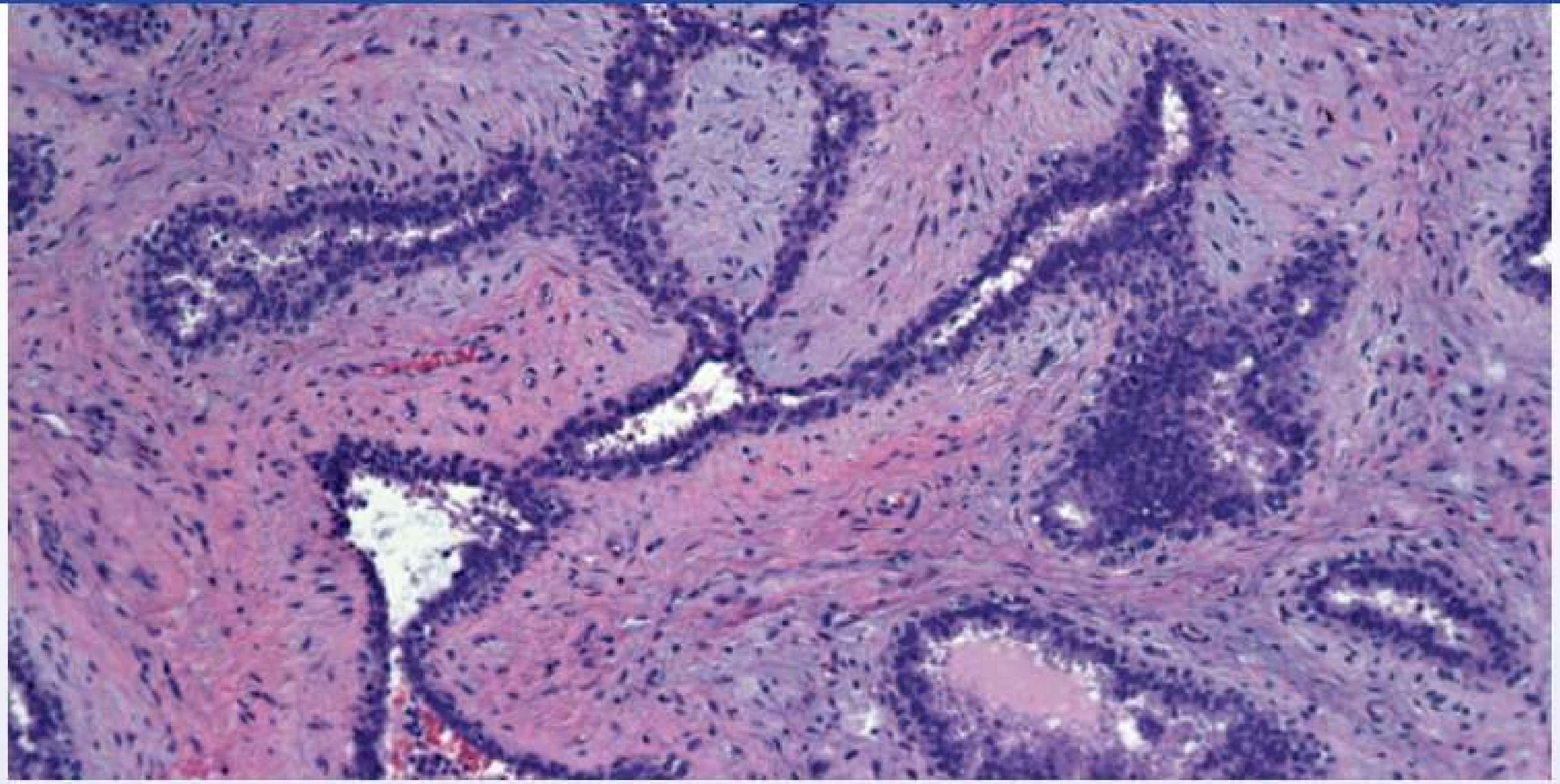

Which of the following is the most likely diagnosis?

- ○ A. Ductal carcinoma in situ
- ○ B. Fibroadenoma
- ○ C. Mammary duct ectasia
- ○ D. Medullary carcinoma
- ○ E. Paget disease of the breast
- ○ F. Sclerosing adenosis

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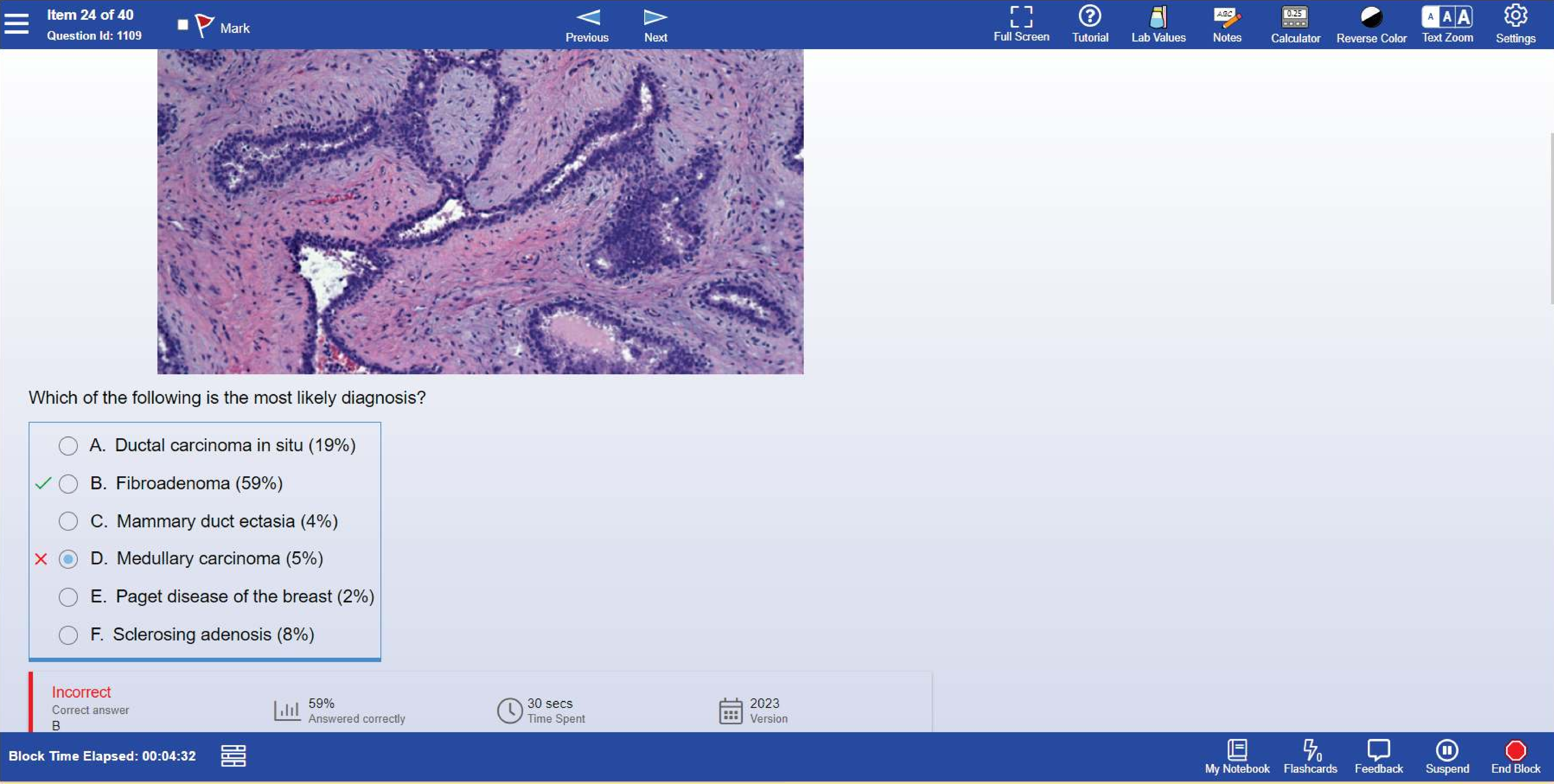
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Which of the following is the most likely diagnosis?

- ○ A. Ductal carcinoma in situ (19%)
- ✓ ○ B. Fibroadenoma (59%)
- ○ C. Mammary duct ectasia (4%)
- ✗ ● D. Medullary carcinoma (5%)
- ○ E. Paget disease of the breast (2%)
- ○ F. Sclerosing adenosis (8%)

Incorrect
Correct answer
B

59%
Answered correctly

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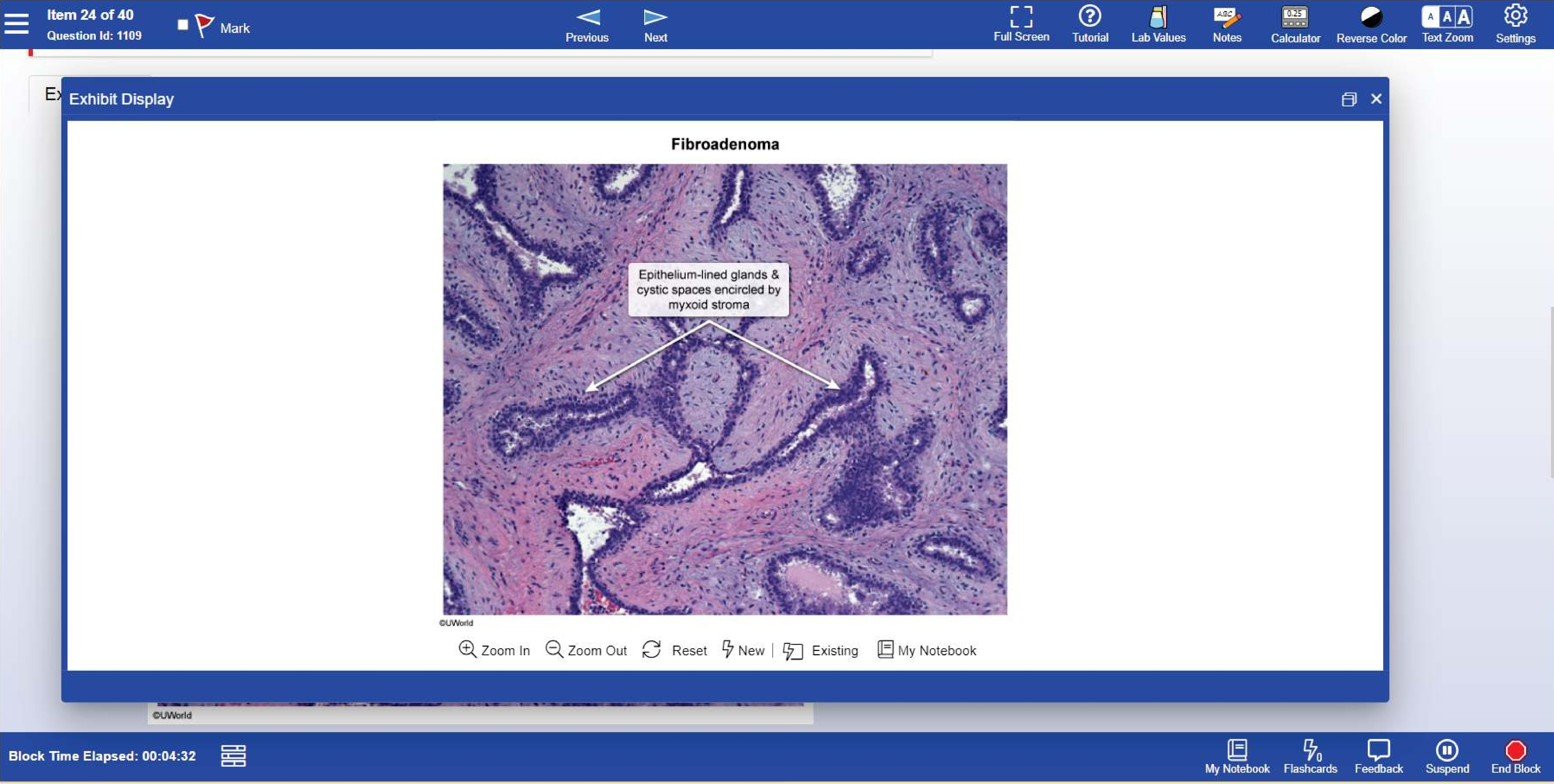
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Fibroadenoma

Epithelium-lined glands & cystic spaces encircled by myxoid stroma

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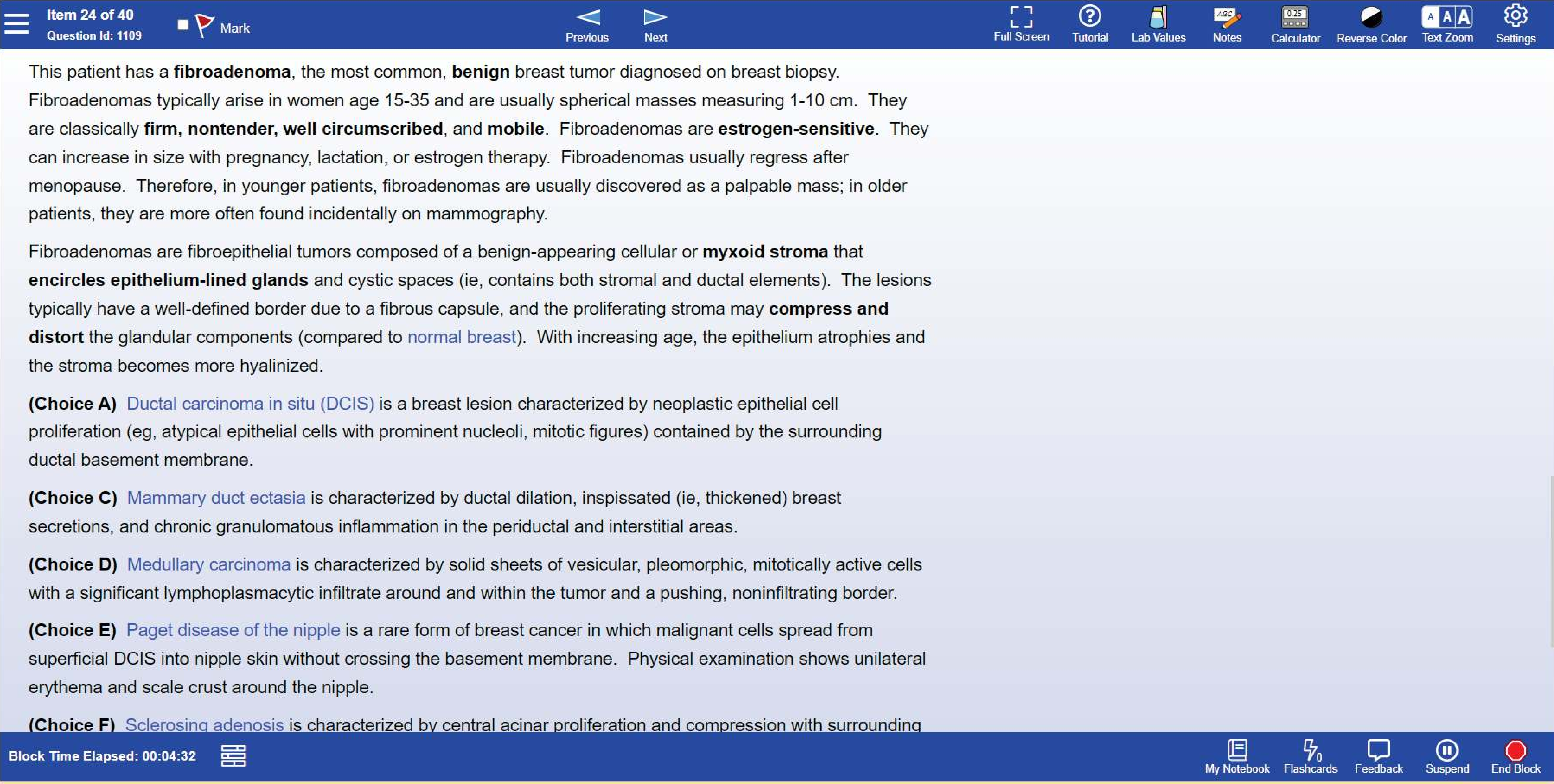


This patient has a **fibroadenoma**, the most common, **benign** breast tumor diagnosed on breast biopsy. Fibroadenomas typically arise in women age 15-35 and are usually spherical masses measuring 1-10 cm. They are classically **firm, nontender, well circumscribed**, and **mobile**. Fibroadenomas are **estrogen-sensitive**. They can increase in size with pregnancy, lactation, or estrogen therapy. Fibroadenomas usually regress after menopause. Therefore, in younger patients, fibroadenomas are usually discovered as a palpable mass; in older patients, they are more often found incidentally on mammography.

Fibroadenomas are fibroepithelial tumors composed of a benign-appearing cellular or **myxoid stroma** that **encircles epithelium-lined glands** and cystic spaces (ie, contains both stromal and ductal elements). The lesions typically have a well-defined border due to a fibrous capsule, and the proliferating stroma may **compress and distort** the glandular components (compared to normal breast). With increasing age, the epithelium atrophies and the stroma becomes more hyalinized.

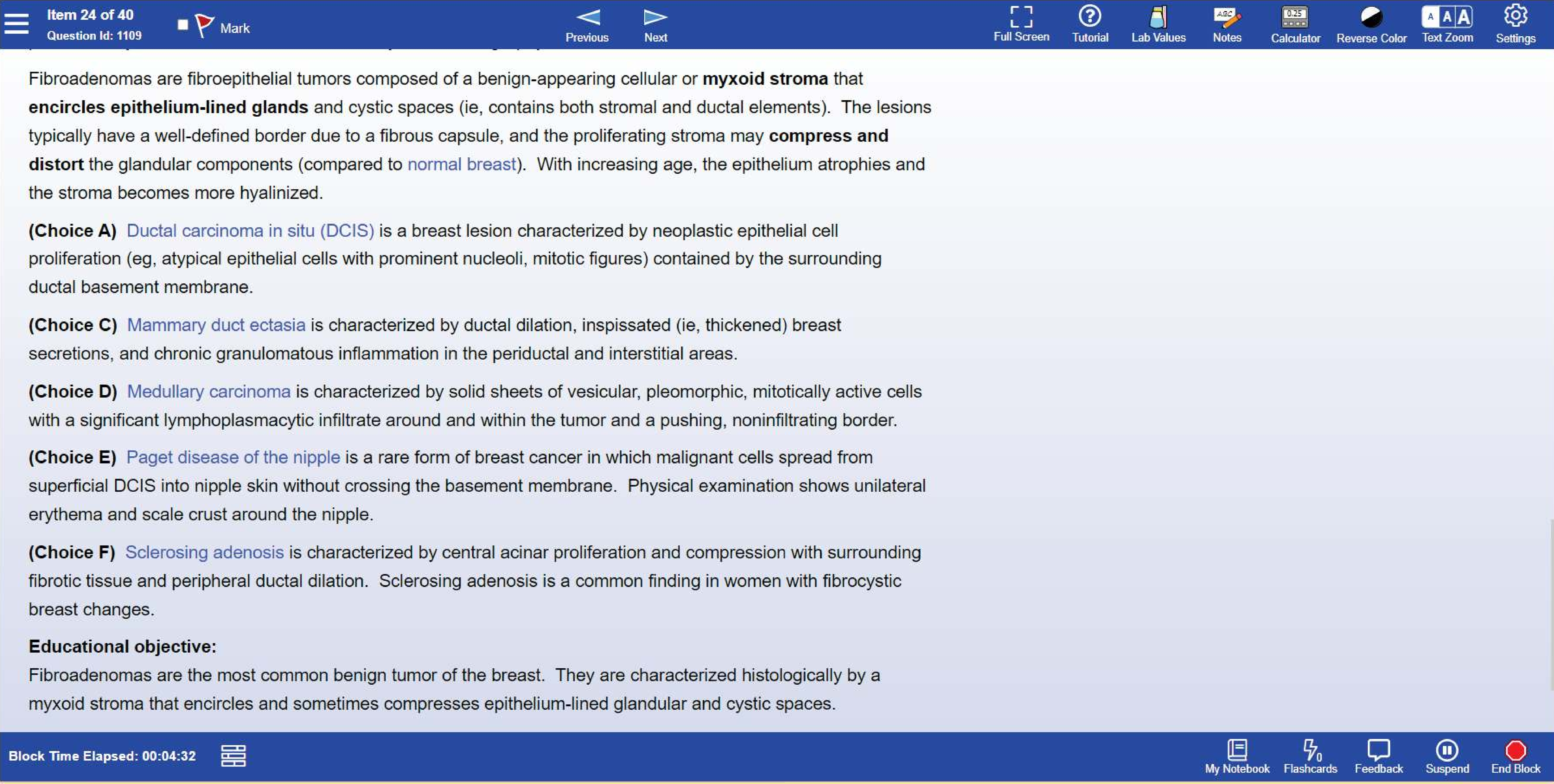
(Choice A) Ductal carcinoma in situ (DCIS) is a breast lesion characterized by neoplastic epithelial cell proliferation (eg, atypical epithelial cells with prominent nucleoli, mitotic figures) contained by the surrounding ductal basement membrane.

(Choice C) Mammary duct ectasia is characterized by ductal dilation, inspissated (ie, thickened) breast secretions, and chronic granulomatous inflammation in the periductal and interstitial areas.

(Choice D) Medullary carcinoma is characterized by solid sheets of vesicular, pleomorphic, mitotically active cells with a significant lymphoplasmacytic infiltrate around and within the tumor and a pushing, noninfiltrating border.

(Choice E) Paget disease of the nipple is a rare form of breast cancer in which malignant cells spread from superficial DCIS into nipple skin without crossing the basement membrane. Physical examination shows unilateral erythema and scale crust around the nipple.

(Choice F) Sclerosing adenosis is characterized by central acinar proliferation and compression with surrounding



Fibroadenomas are fibroepithelial tumors composed of a benign-appearing cellular or **myxoid stroma** that **encircles epithelium-lined glands** and cystic spaces (ie, contains both stromal and ductal elements). The lesions typically have a well-defined border due to a fibrous capsule, and the proliferating stroma may **compress and distort** the glandular components (compared to normal breast). With increasing age, the epithelium atrophies and the stroma becomes more hyalinized.

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(Choice E) Paget disease of the nipple is a rare form of breast cancer in which malignant cells spread from superficial DCIS into nipple skin without crossing the basement membrane. Physical examination shows unilateral erythema and scale crust around the nipple.

(Choice F) Sclerosing adenosis is characterized by central acinar proliferation and compression with surrounding fibrotic tissue and peripheral ductal dilation. Sclerosing adenosis is a common finding in women with fibrocystic breast changes.

Educational objective:

Fibroadenomas are the most common benign tumor of the breast. They are characterized histologically by a myxoid stroma that encircles and sometimes compresses epithelium-lined glandular and cystic spaces.

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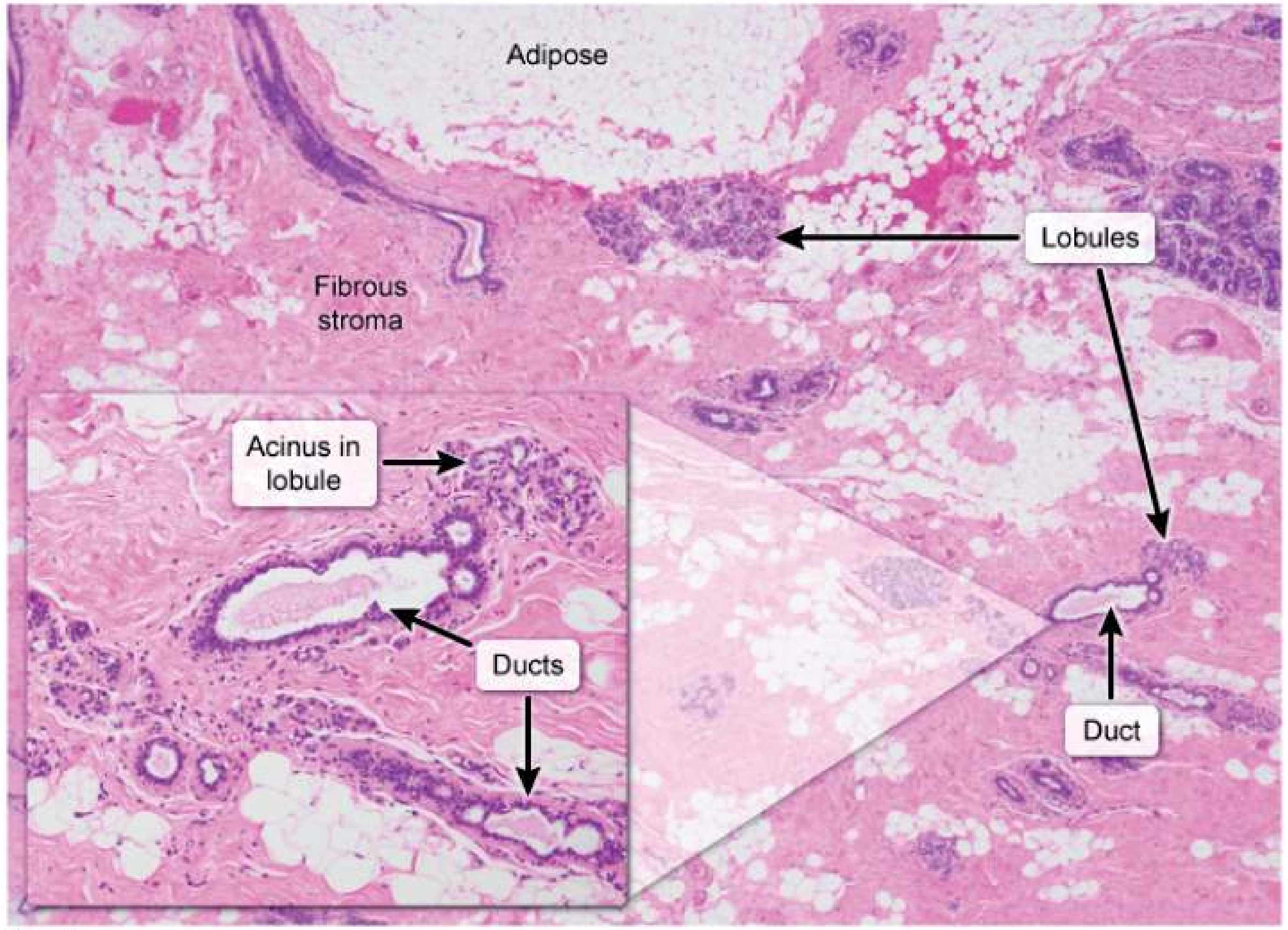
Normal breast tissue


Adipose
Lobules
Fibrous stroma
Acinus in lobule
Ducts
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(Choice E) Paget disease of the nipple is a rare form of breast cancer in which malignant cells spread from

This patient has a **fibroadenoma**, the most common, **benign** breast tumor diagnosed on breast biopsy.

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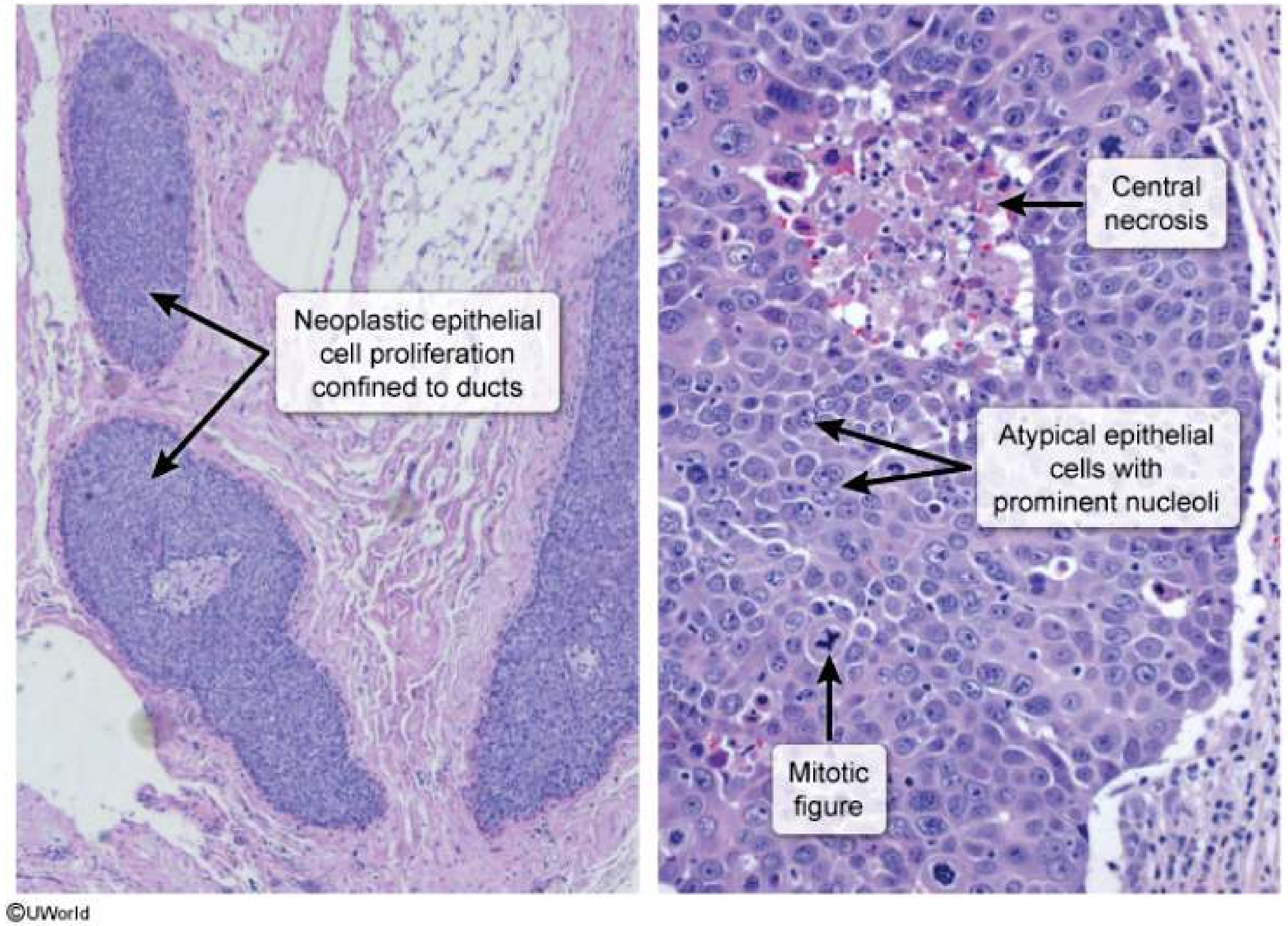
Ductal carcinoma in situ


Neoplastic epithelial cell proliferation confined to ducts
Central necrosis
Atypical epithelial cells with prominent nucleoli
Mitotic figure

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(Choice F) Sclerosing adenosis is characterized by central acinar proliferation and compression with surrounding

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can increase in size with pregnancy, lactation, or estrogen therapy. Fibroadenomas usually regress after

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Educational objective:

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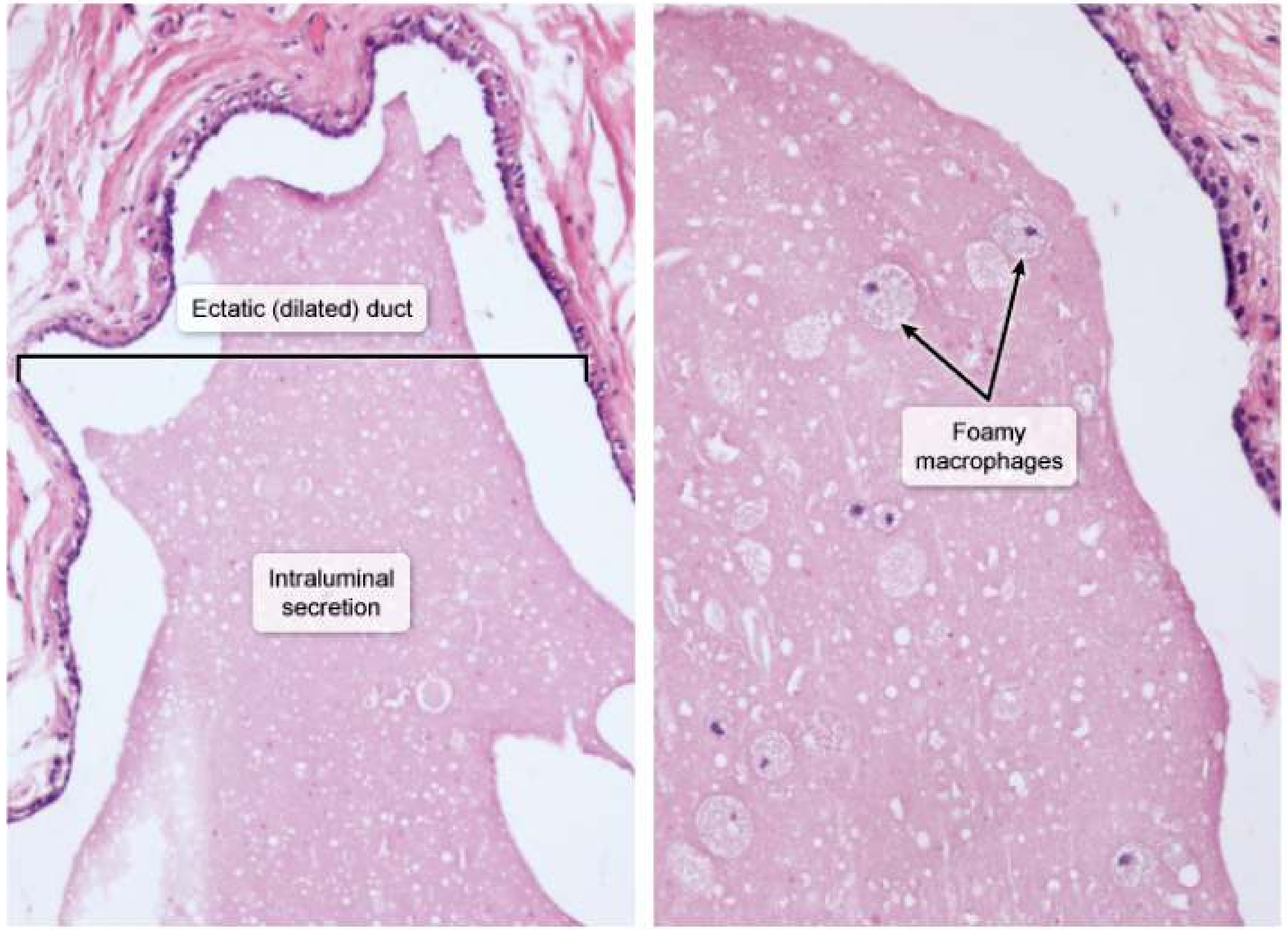
Mammary duct ectasia


Ectatic (dilated) duct
Intraluminal secretion
Foamy macrophages

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Fibroadenomas are fibroepithelial tumors composed of a benign-appearing cellular or **myxoid stroma** that

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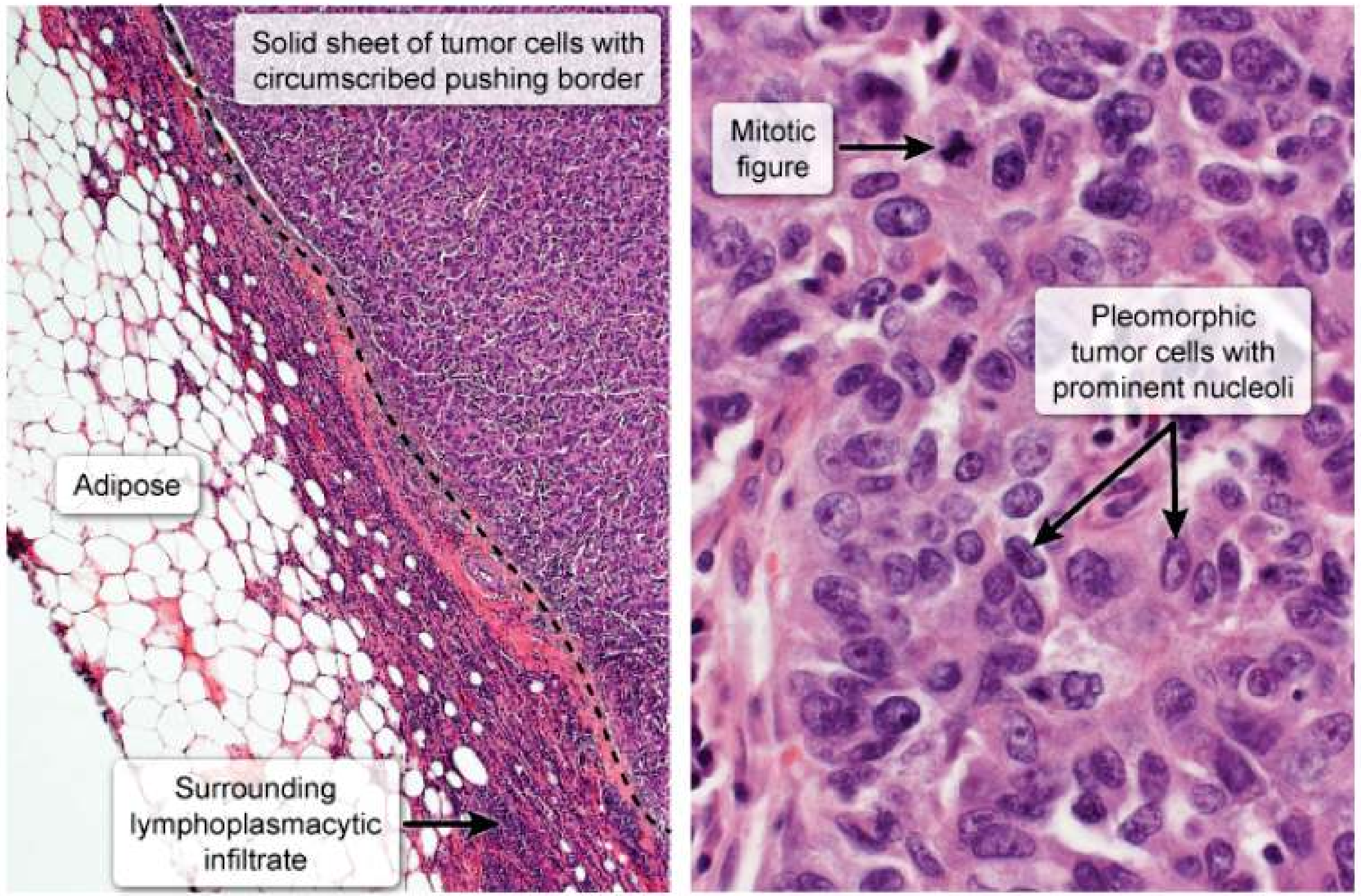
Exhibit Display

Breast carcinoma with medullary features


Solid sheet of tumor cells with circumscribed pushing border
Adipose
Surrounding lymphoplasmacytic infiltrate
Mitotic figure
Pleomorphic tumor cells with prominent nucleoli

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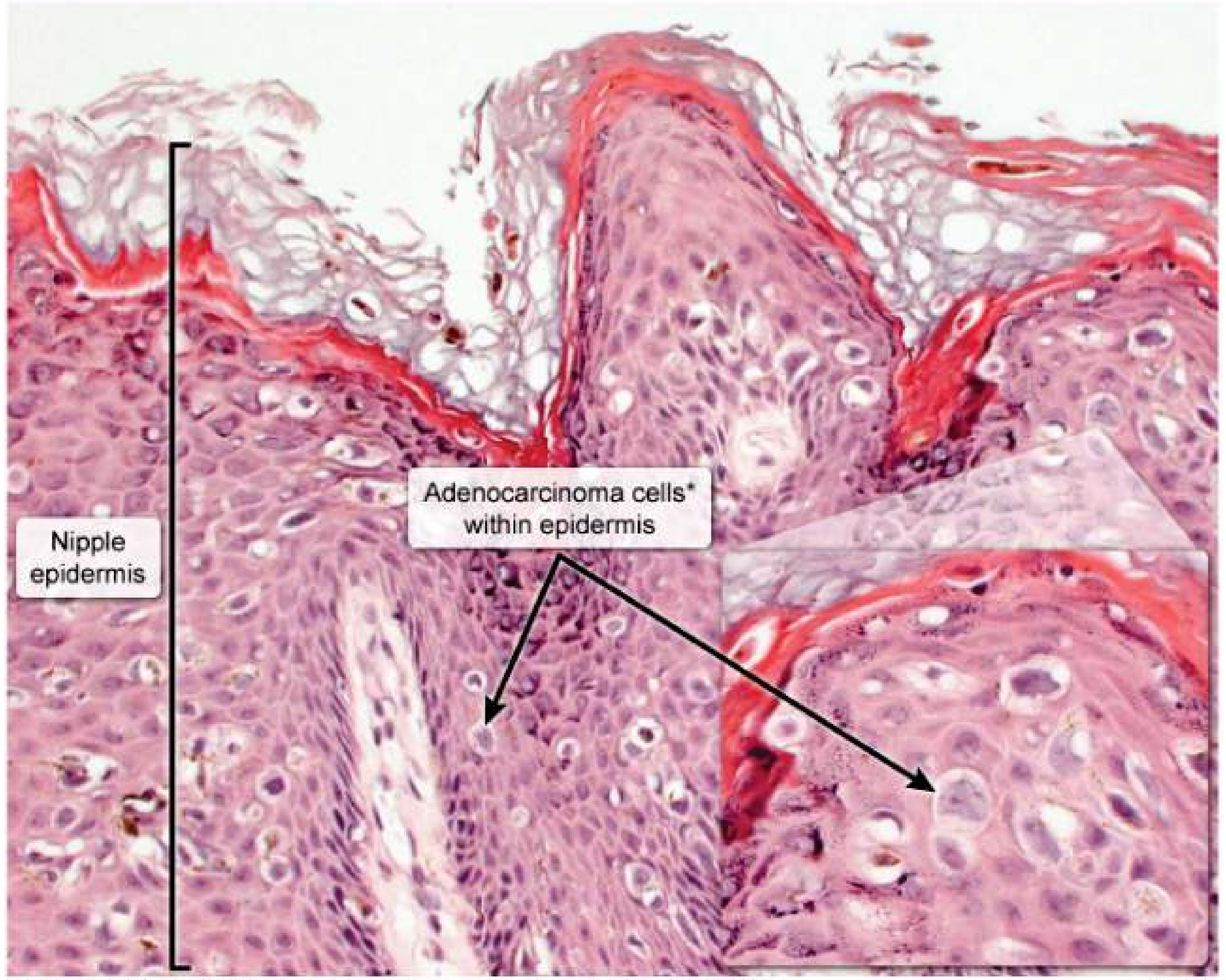
Paget disease of the breast



*Large cells with abundant pale cytoplasm, irregular nuclei, and prominent nucleoli.

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Fibroadenomas are fibroepithelial tumors composed of a benign-appearing cellular or myxoid stroma that

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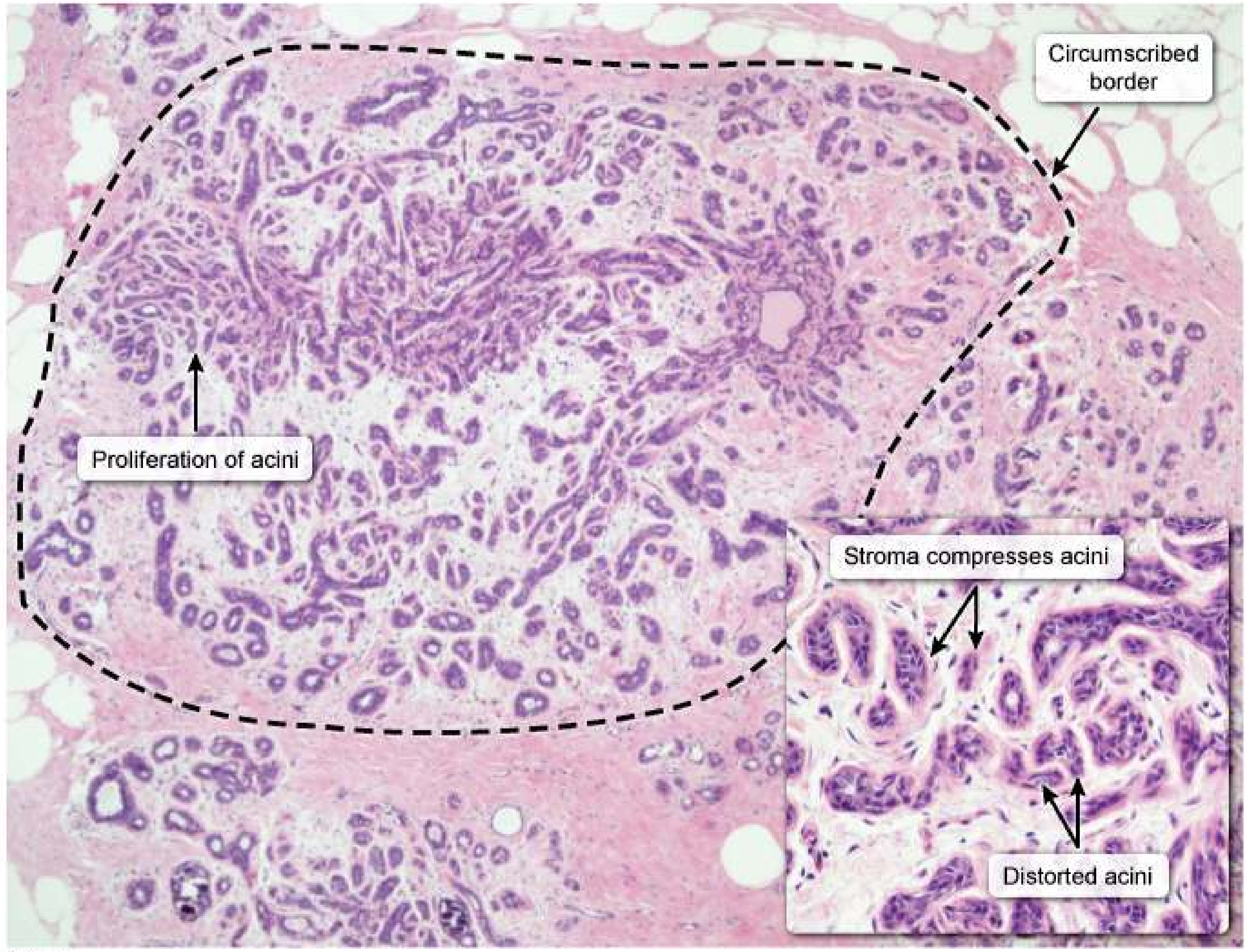
Sclerosing adenosis


Circumscribed border
Proliferation of acini
Stroma compresses acini
Distorted acini

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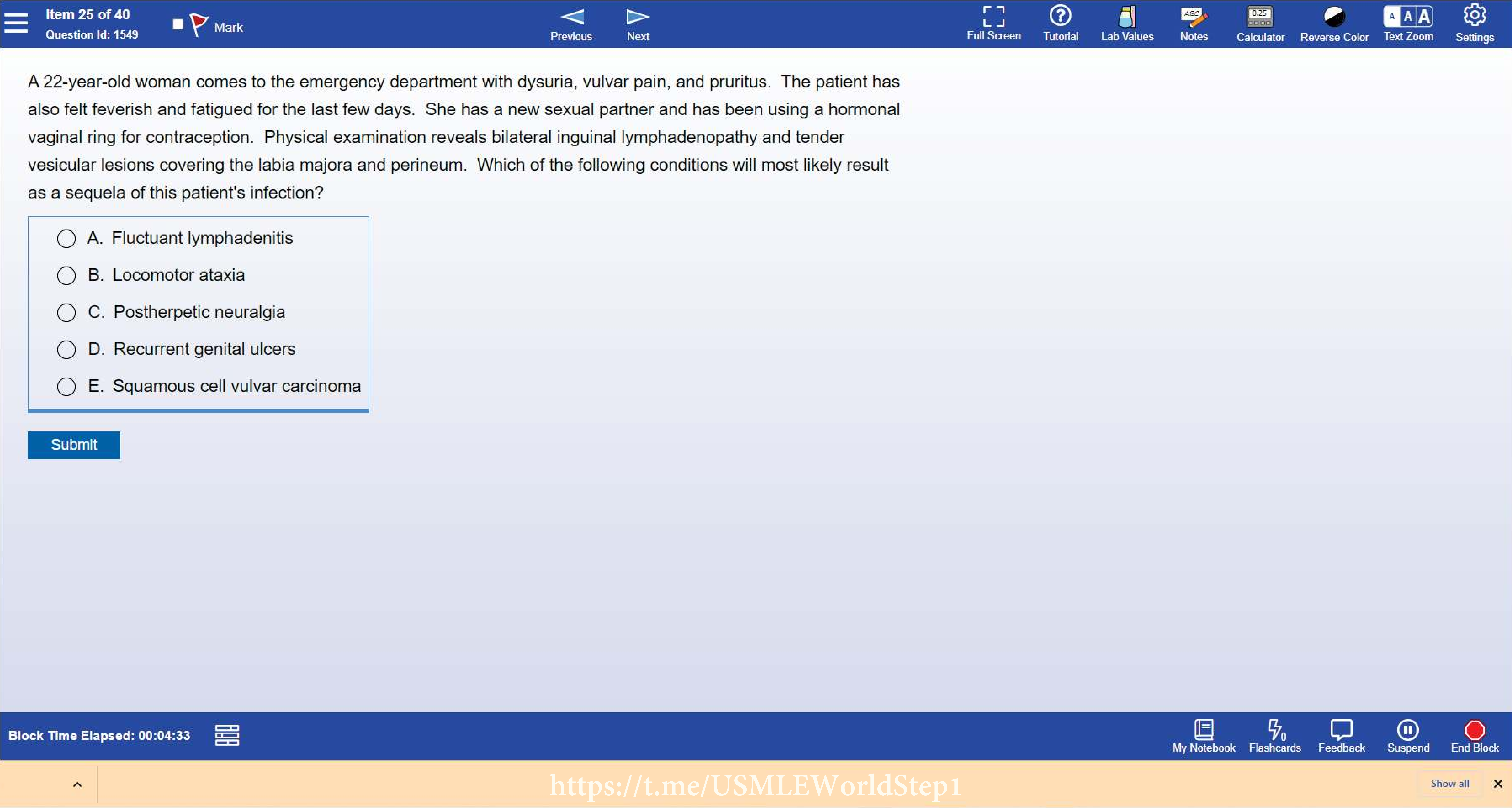
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A 22-year-old woman comes to the emergency department with dysuria, vulvar pain, and pruritus. The patient has also felt feverish and fatigued for the last few days. She has a new sexual partner and has been using a hormonal vaginal ring for contraception. Physical examination reveals bilateral inguinal lymphadenopathy and tender vesicular lesions covering the labia majora and perineum. Which of the following conditions will most likely result as a sequela of this patient's infection?

○ A. Fluctuant lymphadenitis
○ B. Locomotor ataxia
○ C. Postherpetic neuralgia
○ D. Recurrent genital ulcers
○ E. Squamous cell vulvar carcinoma

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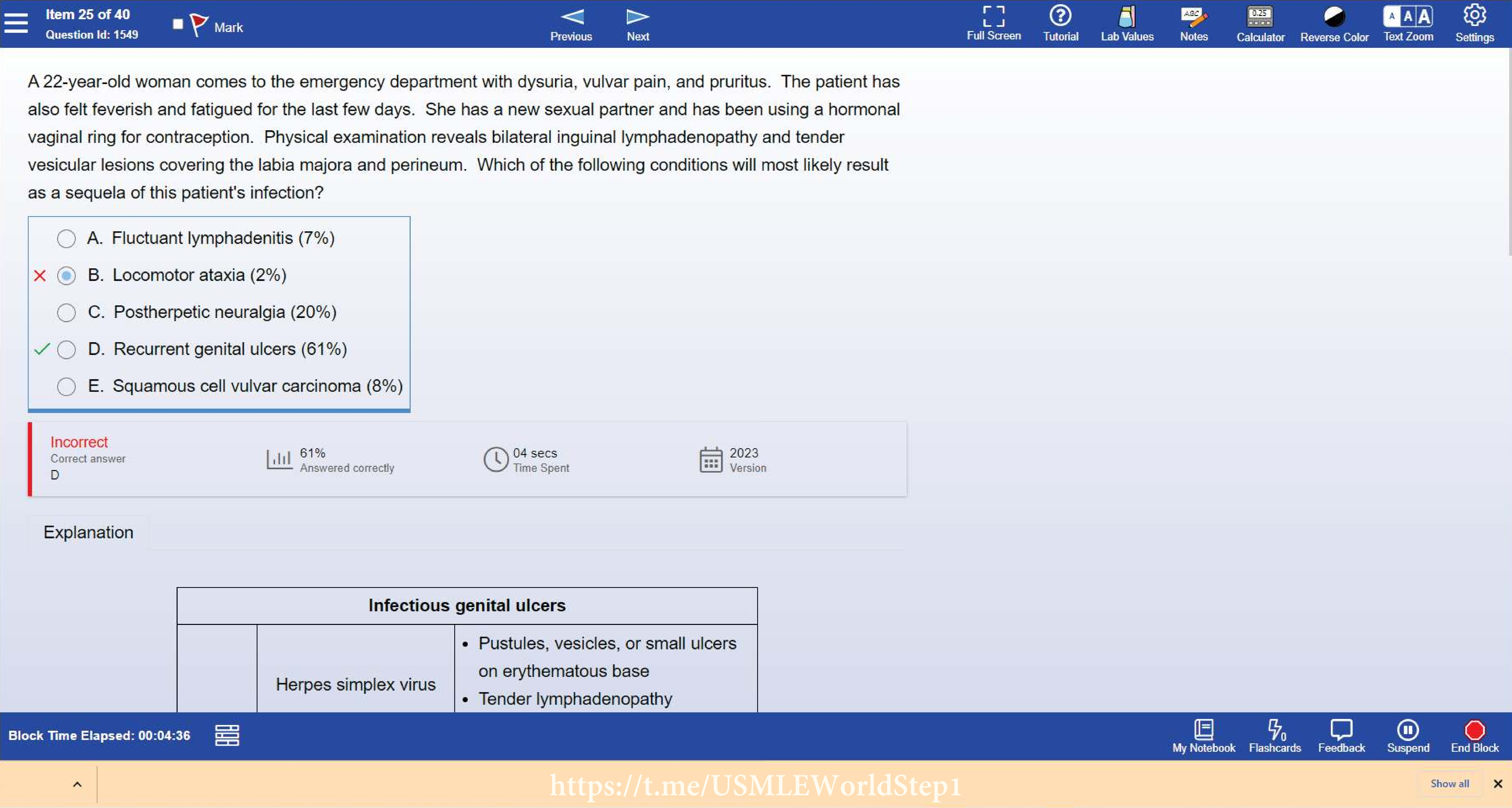
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A 22-year-old woman comes to the emergency department with dysuria, vulvar pain, and pruritus. The patient has also felt feverish and fatigued for the last few days. She has a new sexual partner and has been using a hormonal vaginal ring for contraception. Physical examination reveals bilateral inguinal lymphadenopathy and tender vesicular lesions covering the labia majora and perineum. Which of the following conditions will most likely result as a sequela of this patient's infection?

- ○ A. Fluctuant lymphadenitis (7%)
- ✗ ● B. Locomotor ataxia (2%)
- ○ C. Postherpetic neuralgia (20%)
- ✓ ○ D. Recurrent genital ulcers (61%)
- ○ E. Squamous cell vulvar carcinoma (8%)

Incorrect
Correct answer
D

61%
Answered correctly

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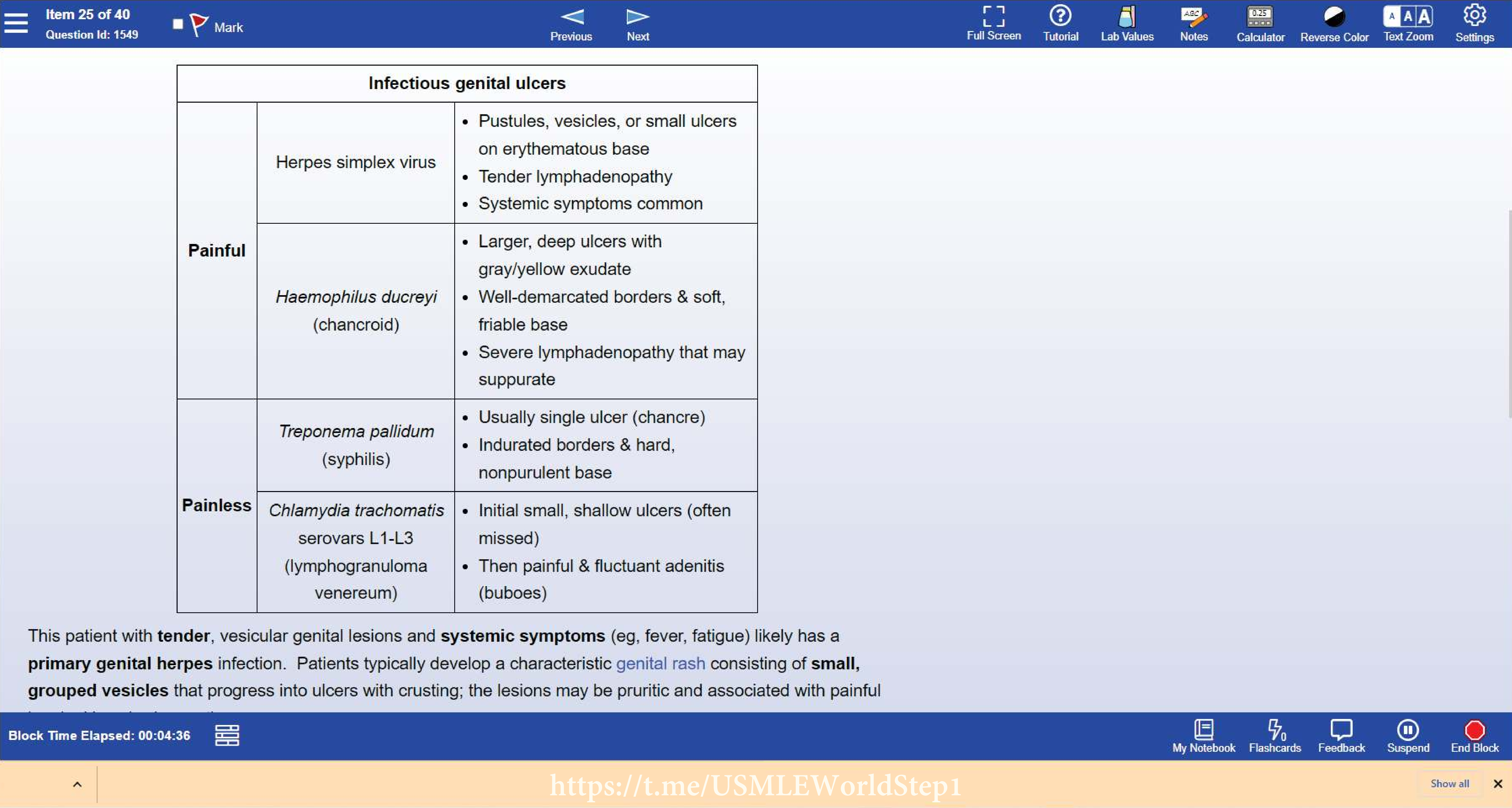
Explanation

Infectious genital ulcers		
	Herpes simplex virus	• Pustules, vesicles, or small ulcers on erythematous base • Tender lymphadenopathy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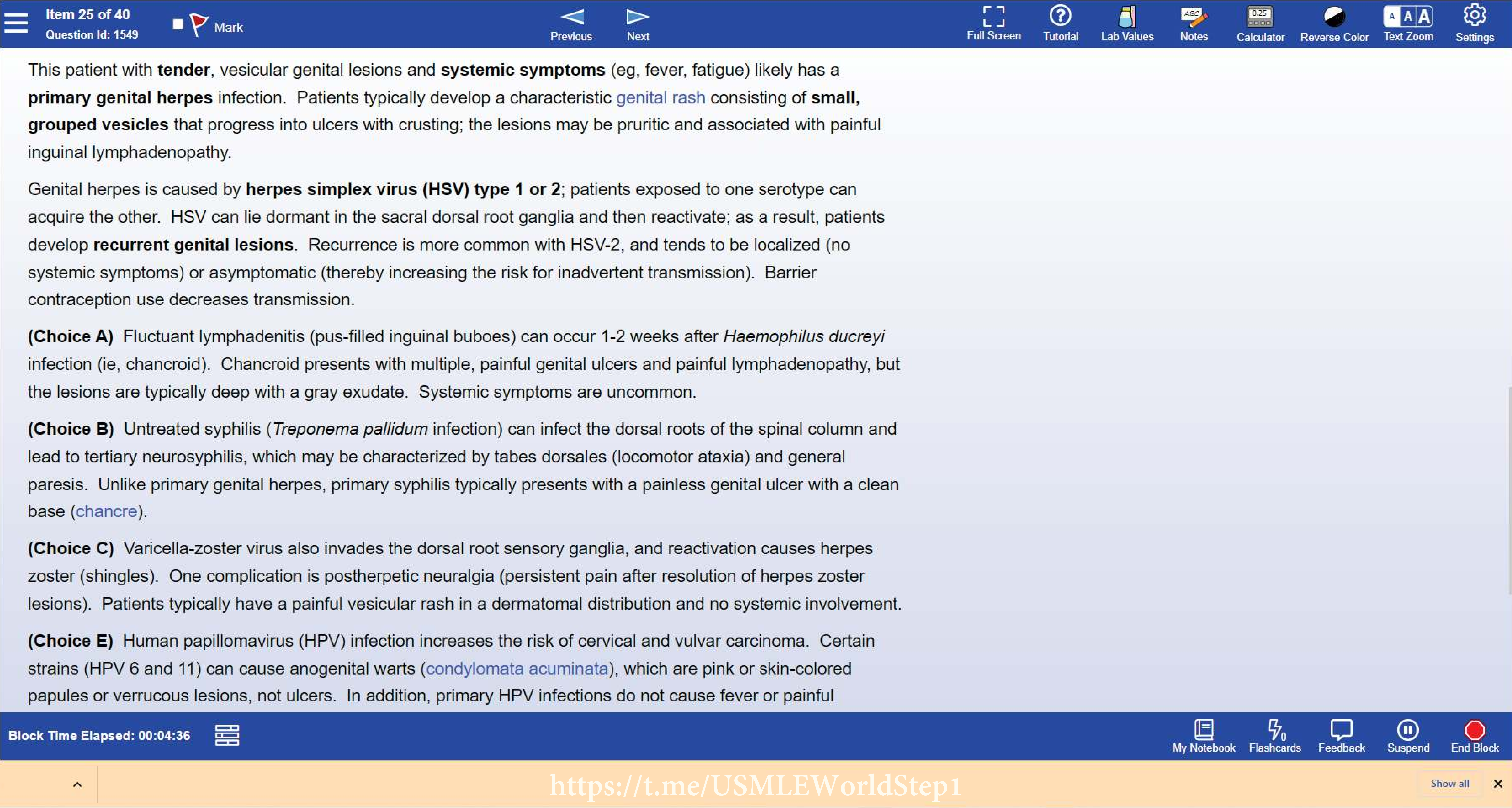
Infectious genital ulcers		
Painful	Herpes simplex virus	- Pustules, vesicles, or small ulcers on erythematous base - Tender lymphadenopathy - Systemic symptoms common
	Haemophilus ducreyi (chancroid)	- Larger, deep ulcers with gray/yellow exudate - Well-demarcated borders & soft, friable base - Severe lymphadenopathy that may suppurate
Painless	*Treponema pallidum* (syphilis)	- Usually single ulcer (chancre) - Indurated borders & hard, nonpurulent base
	Chlamydia trachomatis serovars L1-L3 (lymphogranuloma venereum)	- Initial small, shallow ulcers (often missed) - Then painful & fluctuant adenitis (buboes)

This patient with **tender**, vesicular genital lesions and **systemic symptoms** (eg, fever, fatigue) likely has a **primary genital herpes** infection. Patients typically develop a characteristic genital rash consisting of **small, grouped vesicles** that progress into ulcers with crusting; the lesions may be pruritic and associated with painful



This patient with **tender**, vesicular genital lesions and **systemic symptoms** (eg, fever, fatigue) likely has a **primary genital herpes** infection. Patients typically develop a characteristic genital rash consisting of **small, grouped vesicles** that progress into ulcers with crusting; the lesions may be pruritic and associated with painful inguinal lymphadenopathy.

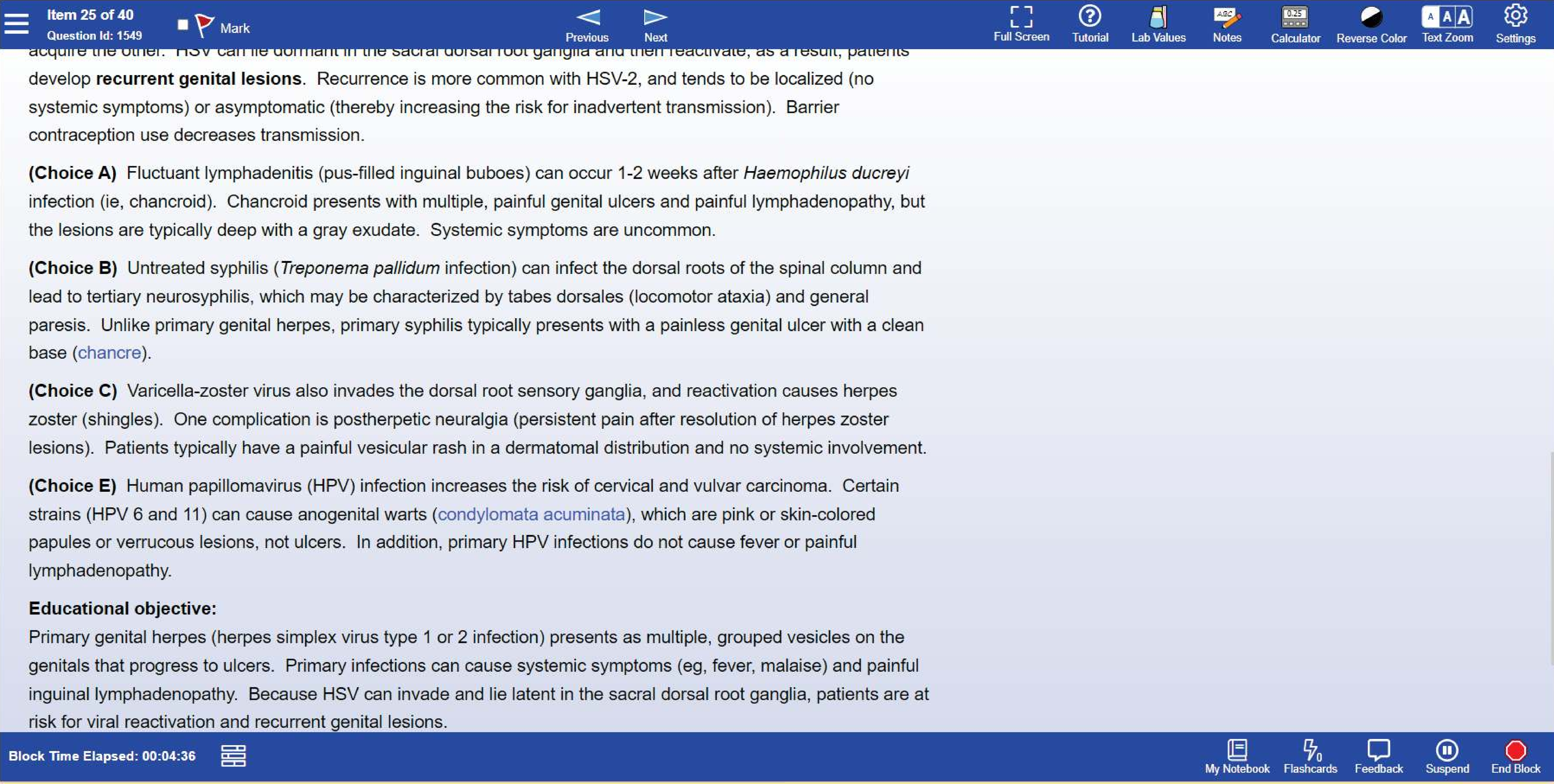
Genital herpes is caused by **herpes simplex virus (HSV) type 1 or 2**; patients exposed to one serotype can acquire the other. HSV can lie dormant in the sacral dorsal root ganglia and then reactivate; as a result, patients develop **recurrent genital lesions**. Recurrence is more common with HSV-2, and tends to be localized (no systemic symptoms) or asymptomatic (thereby increasing the risk for inadvertent transmission). Barrier contraception use decreases transmission.

(Choice A) Fluctuant lymphadenitis (pus-filled inguinal buboes) can occur 1-2 weeks after *Haemophilus ducreyi* infection (ie, chancroid). Chancroid presents with multiple, painful genital ulcers and painful lymphadenopathy, but the lesions are typically deep with a gray exudate. Systemic symptoms are uncommon.

(Choice B) Untreated syphilis (*Treponema pallidum* infection) can infect the dorsal roots of the spinal column and lead to tertiary neurosyphilis, which may be characterized by tabes dorsales (locomotor ataxia) and general paresis. Unlike primary genital herpes, primary syphilis typically presents with a painless genital ulcer with a clean base (chancre).

(Choice C) Varicella-zoster virus also invades the dorsal root sensory ganglia, and reactivation causes herpes zoster (shingles). One complication is postherpetic neuralgia (persistent pain after resolution of herpes zoster lesions). Patients typically have a painful vesicular rash in a dermatomal distribution and no systemic involvement.

(Choice E) Human papillomavirus (HPV) infection increases the risk of cervical and vulvar carcinoma. Certain strains (HPV 6 and 11) can cause anogenital warts (condylomata acuminata), which are pink or skin-colored papules or verrucous lesions, not ulcers. In addition, primary HPV infections do not cause fever or painful



acquire the other. HSV can lie dormant in the sacral dorsal root ganglia and then reactivate; as a result, patients develop **recurrent genital lesions**. Recurrence is more common with HSV-2, and tends to be localized (no systemic symptoms) or asymptomatic (thereby increasing the risk for inadvertent transmission). Barrier contraception use decreases transmission.

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(Choice B) Untreated syphilis (*Treponema pallidum* infection) can infect the dorsal roots of the spinal column and lead to tertiary neurosyphilis, which may be characterized by tabes dorsales (locomotor ataxia) and general paresis. Unlike primary genital herpes, primary syphilis typically presents with a painless genital ulcer with a clean base (chancre).

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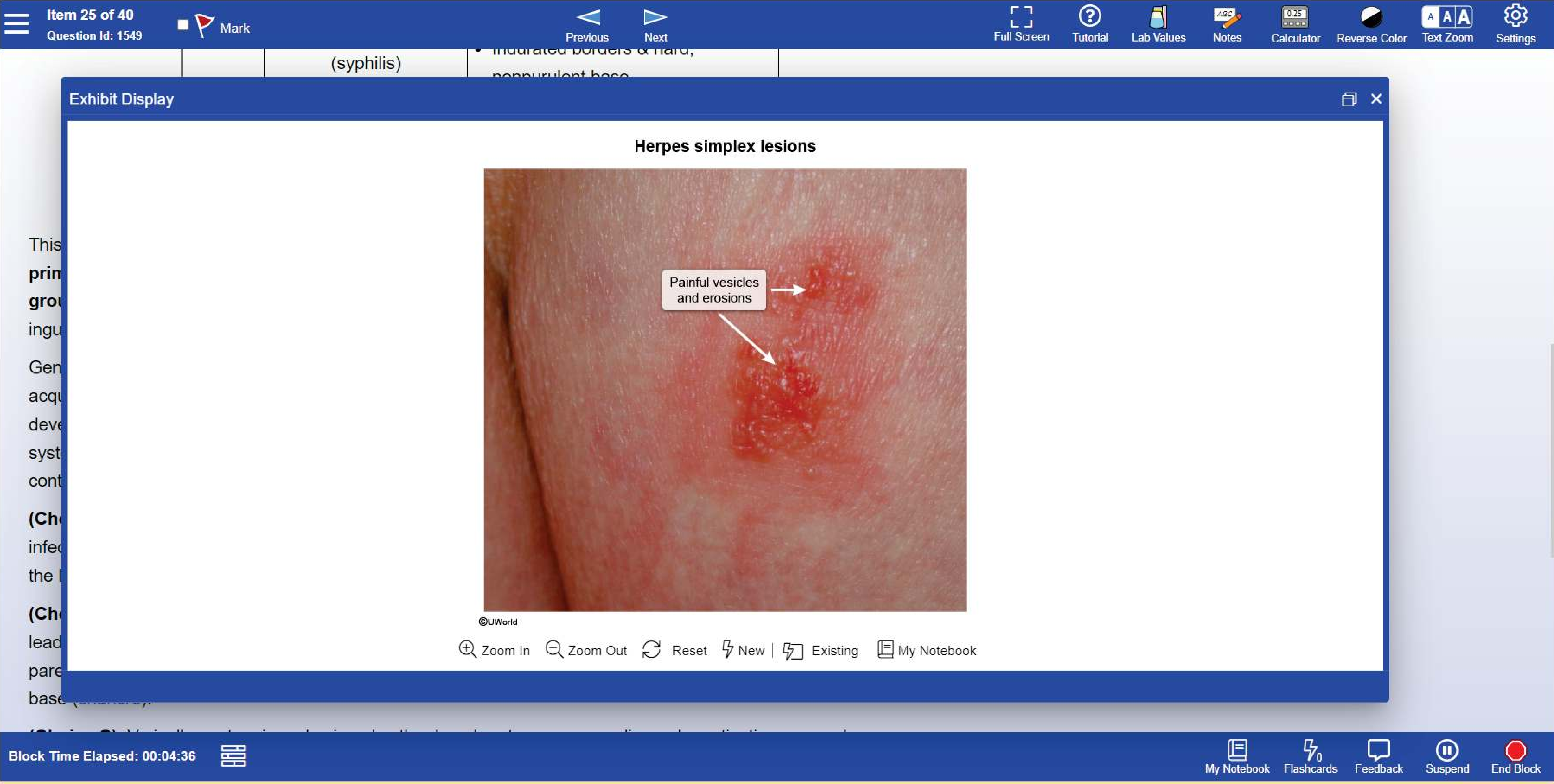
(Choice E) Human papillomavirus (HPV) infection increases the risk of cervical and vulvar carcinoma. Certain strains (HPV 6 and 11) can cause anogenital warts (condylomata acuminata), which are pink or skin-colored papules or verrucous lesions, not ulcers. In addition, primary HPV infections do not cause fever or painful lymphadenopathy.

Educational objective:

Primary genital herpes (herpes simplex virus type 1 or 2 infection) presents as multiple, grouped vesicles on the genitals that progress to ulcers. Primary infections can cause systemic symptoms (eg, fever, malaise) and painful inguinal lymphadenopathy. Because HSV can invade and lie latent in the sacral dorsal root ganglia, patients are at risk for viral reactivation and recurrent genital lesions.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(syphilis)

- Indurated borders & hard, nonpurulent base

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Herpes simplex lesions

Painful vesicles and erosions
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This patient with **tender**, vesicular genital lesions and **systemic symptoms** (eg, fever, fatigue) likely has a

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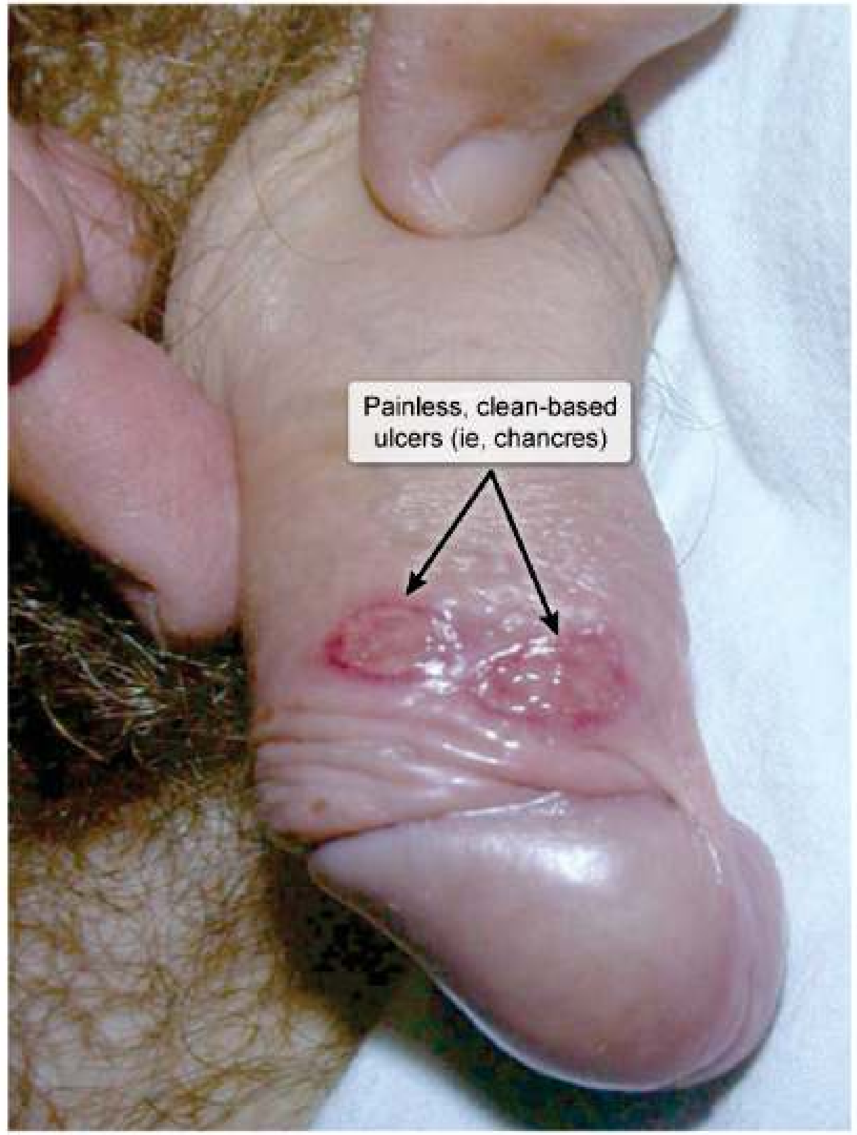
Primary syphilis



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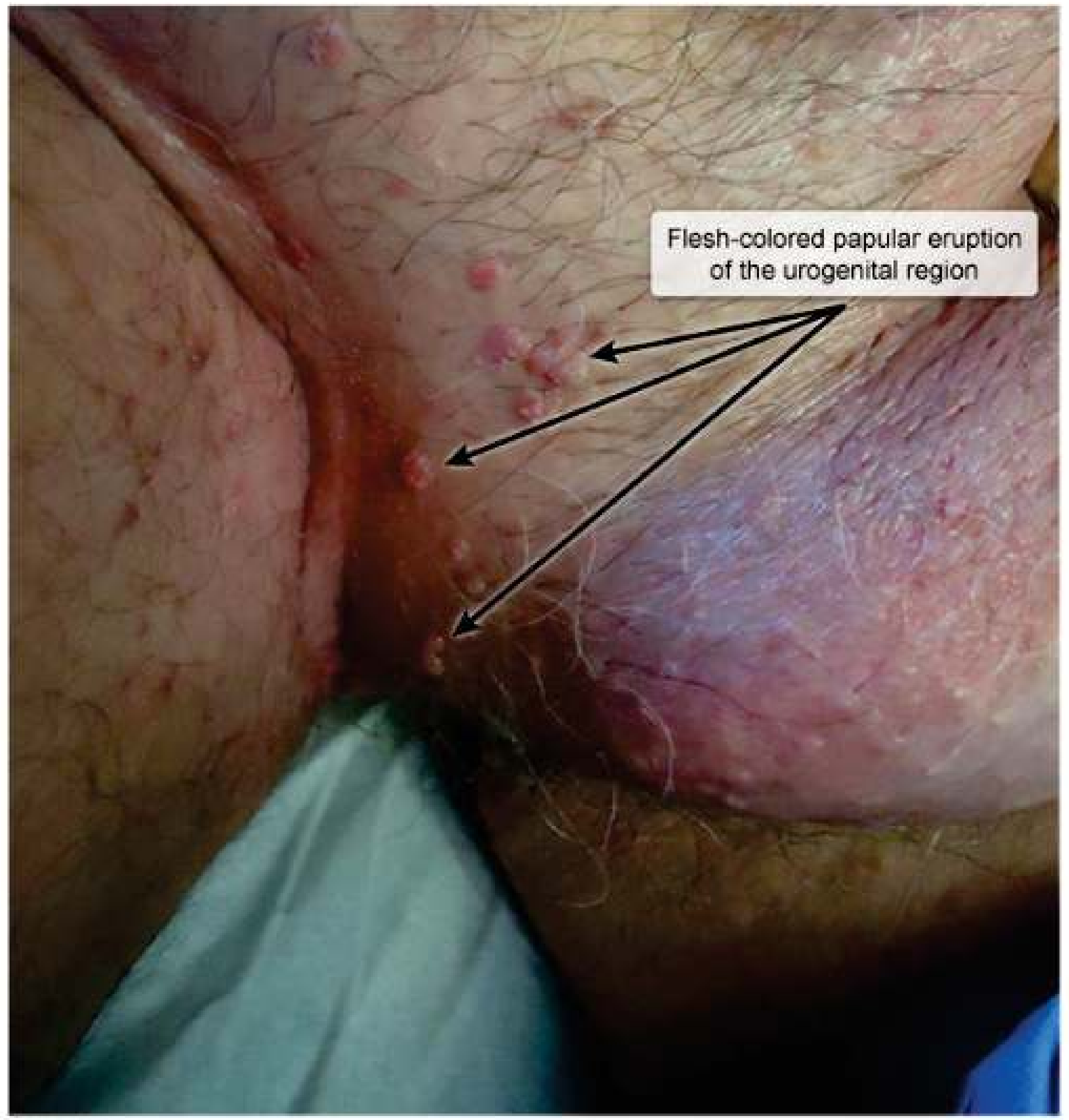
Condylomata acuminata



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risk for viral reactivation and recurrent genital lesions.

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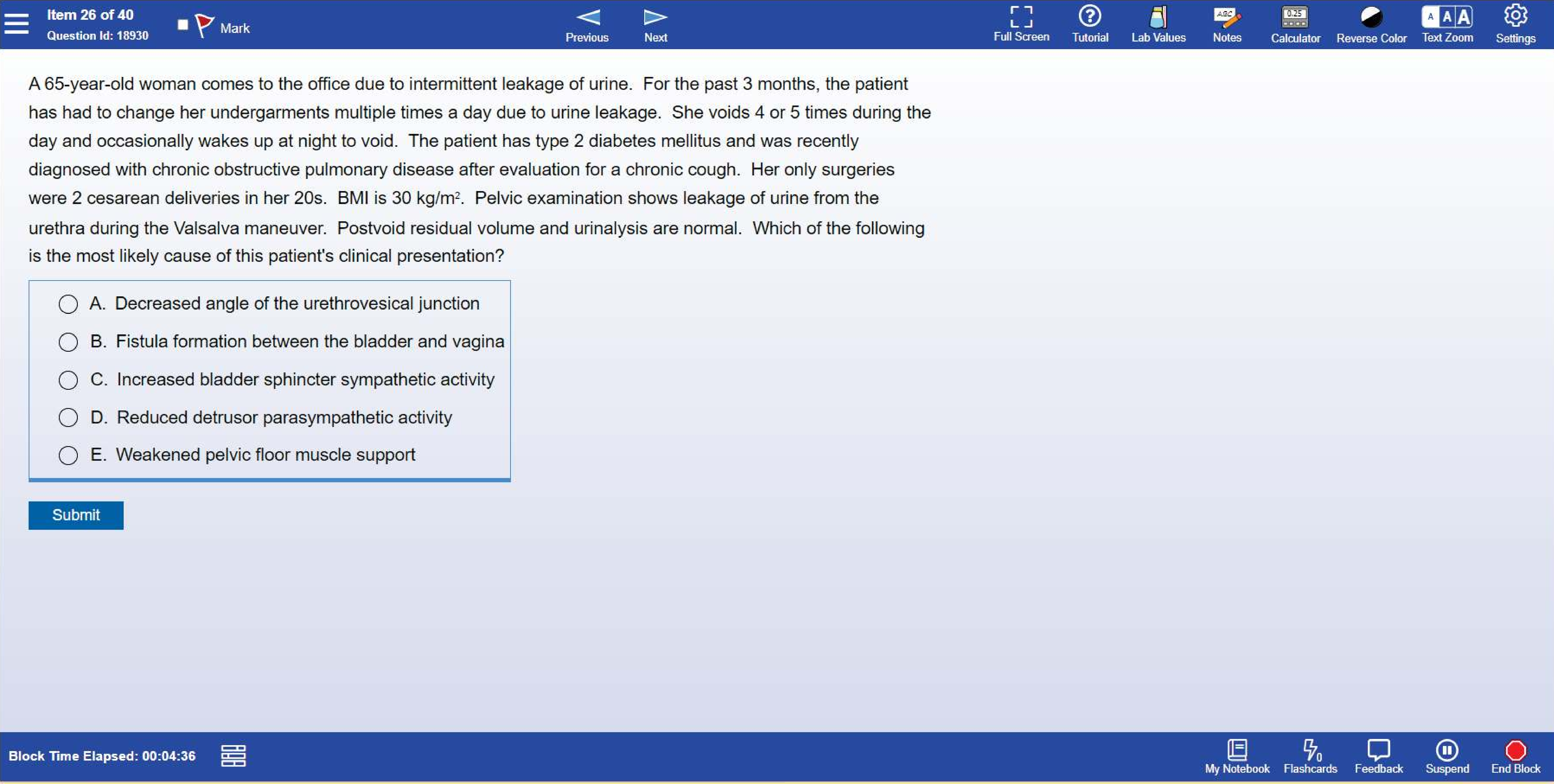
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A 65-year-old woman comes to the office due to intermittent leakage of urine. For the past 3 months, the patient has had to change her undergarments multiple times a day due to urine leakage. She voids 4 or 5 times during the day and occasionally wakes up at night to void. The patient has type 2 diabetes mellitus and was recently diagnosed with chronic obstructive pulmonary disease after evaluation for a chronic cough. Her only surgeries were 2 cesarean deliveries in her 20s. BMI is 30 kg/m^2. Pelvic examination shows leakage of urine from the urethra during the Valsalva maneuver. Postvoid residual volume and urinalysis are normal. Which of the following is the most likely cause of this patient's clinical presentation?

- ○ A. Decreased angle of the urethrovesical junction
- ○ B. Fistula formation between the bladder and vagina
- ○ C. Increased bladder sphincter sympathetic activity
- ○ D. Reduced detrusor parasympathetic activity
- ○ E. Weakened pelvic floor muscle support

Submit

A 65-year-old woman comes to the office due to intermittent leakage of urine. For the past 3 months, the patient has had to change her undergarments multiple times a day due to urine leakage. She voids 4 or 5 times during the day and occasionally wakes up at night to void. The patient has type 2 diabetes mellitus and was recently diagnosed with chronic obstructive pulmonary disease after evaluation for a chronic cough. Her only surgeries were 2 cesarean deliveries in her 20s. BMI is 30 kg/m². Pelvic examination shows leakage of urine from the urethra during the Valsalva maneuver. Postvoid residual volume and urinalysis are normal. Which of the following is the most likely cause of this patient's clinical presentation?

- ○ A. Decreased angle of the urethrovesical junction (4%)
- ✗ ● B. Fistula formation between the bladder and vagina (1%)
- ○ C. Increased bladder sphincter sympathetic activity (5%)
- ○ D. Reduced detrusor parasympathetic activity (11%)
- ✓ ○ E. Weakened pelvic floor muscle support (77%)

Incorrect
Correct answer
E

77%
Answered correctly

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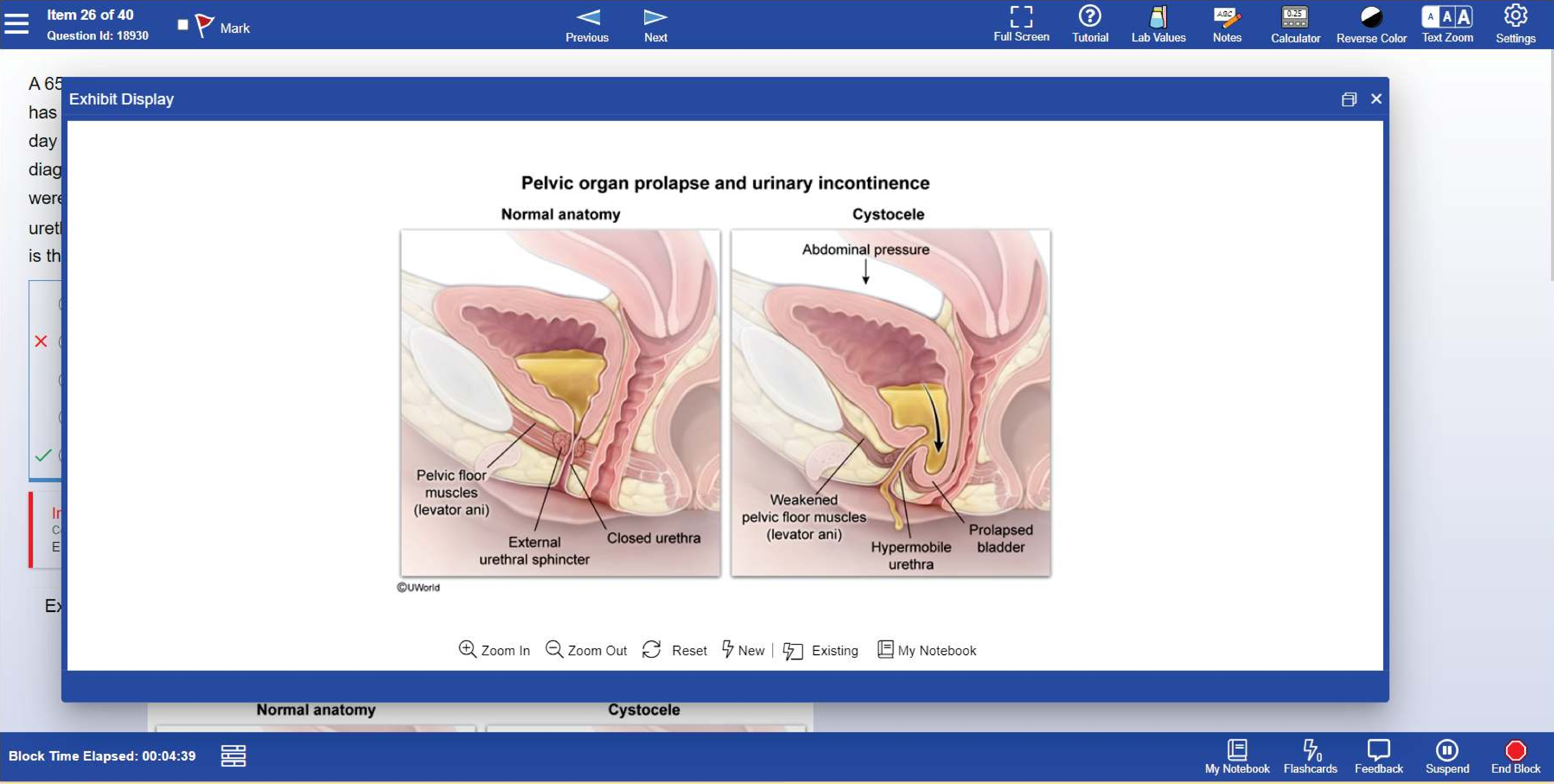
Explanation

Pelvic organ prolapse and urinary incontinence

Normal anatomy
Cystocele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Pelvic organ prolapse and urinary incontinence

Normal anatomy
Pelvic floor muscles (levator ani)
External urethral sphincter
Closed urethra
Cystocele
Abdominal pressure
Weakened pelvic floor muscles (levator ani)
Hypermobile urethra
Prolapsed bladder

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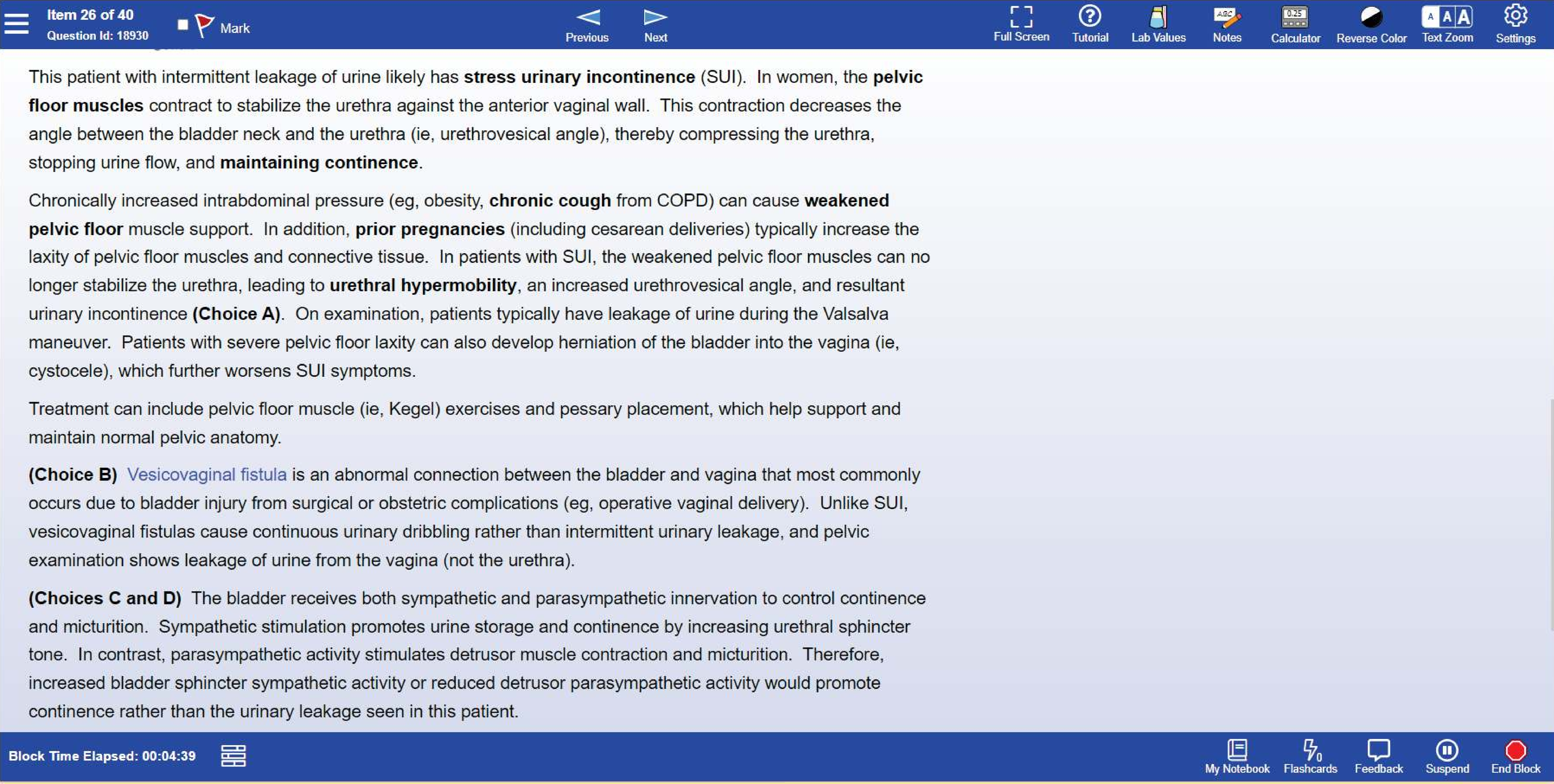


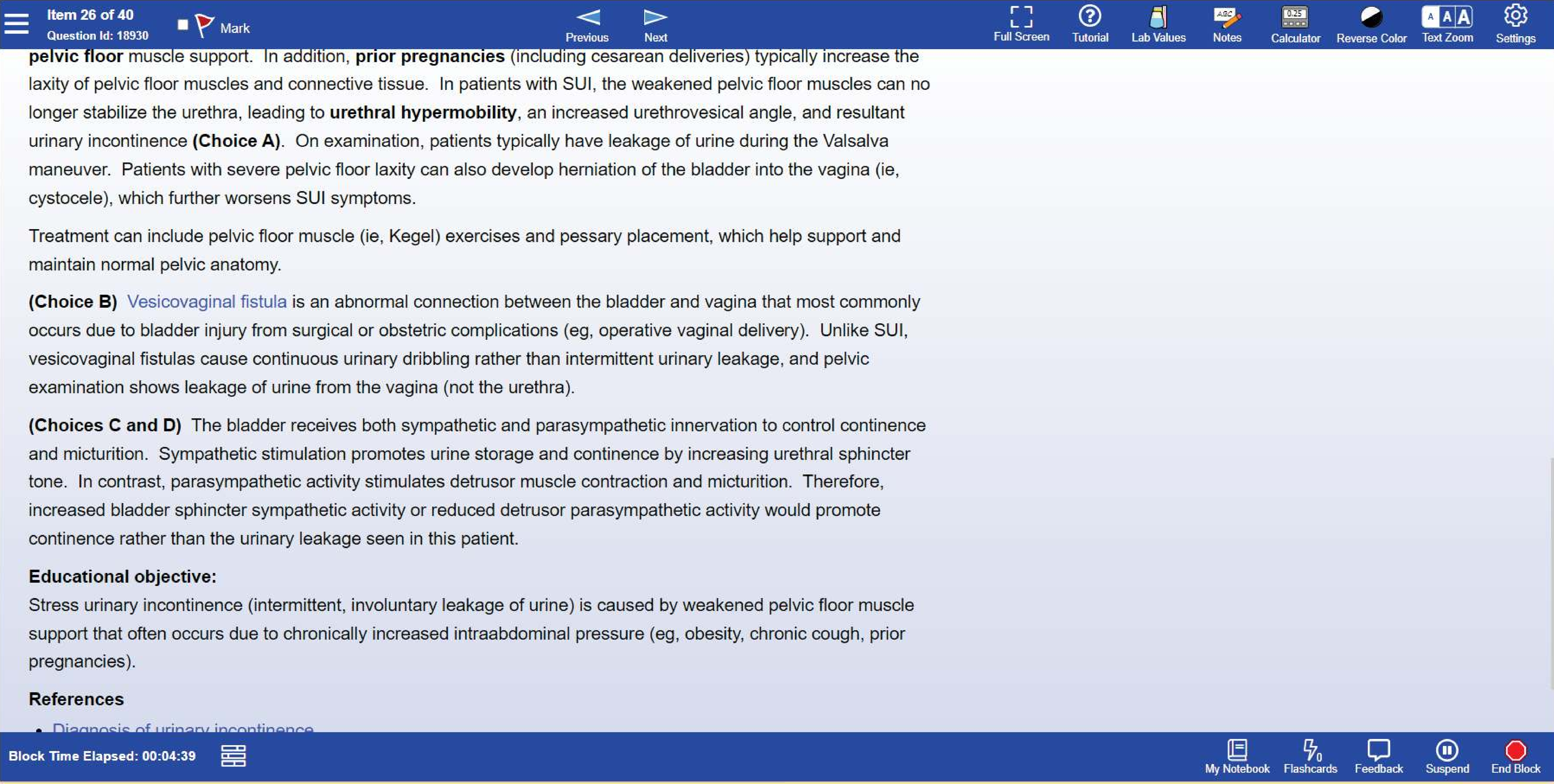
This patient with intermittent leakage of urine likely has **stress urinary incontinence** (SUI). In women, the **pelvic floor muscles** contract to stabilize the urethra against the anterior vaginal wall. This contraction decreases the angle between the bladder neck and the urethra (ie, urethrovesical angle), thereby compressing the urethra, stopping urine flow, and **maintaining continence**.

Chronically increased intrabdominal pressure (eg, obesity, **chronic cough** from COPD) can cause **weakened pelvic floor** muscle support. In addition, **prior pregnancies** (including cesarean deliveries) typically increase the laxity of pelvic floor muscles and connective tissue. In patients with SUI, the weakened pelvic floor muscles can no longer stabilize the urethra, leading to **urethral hypermobility**, an increased urethrovesical angle, and resultant urinary incontinence **(Choice A)**. On examination, patients typically have leakage of urine during the Valsalva maneuver. Patients with severe pelvic floor laxity can also develop herniation of the bladder into the vagina (ie, cystocele), which further worsens SUI symptoms.

Treatment can include pelvic floor muscle (ie, Kegel) exercises and pessary placement, which help support and maintain normal pelvic anatomy.

(Choice B) Vesicovaginal fistula is an abnormal connection between the bladder and vagina that most commonly occurs due to bladder injury from surgical or obstetric complications (eg, operative vaginal delivery). Unlike SUI, vesicovaginal fistulas cause continuous urinary dribbling rather than intermittent urinary leakage, and pelvic examination shows leakage of urine from the vagina (not the urethra).

(Choices C and D) The bladder receives both sympathetic and parasympathetic innervation to control continence and micturition. Sympathetic stimulation promotes urine storage and continence by increasing urethral sphincter tone. In contrast, parasympathetic activity stimulates detrusor muscle contraction and micturition. Therefore, increased bladder sphincter sympathetic activity or reduced detrusor parasympathetic activity would promote continence rather than the urinary leakage seen in this patient.



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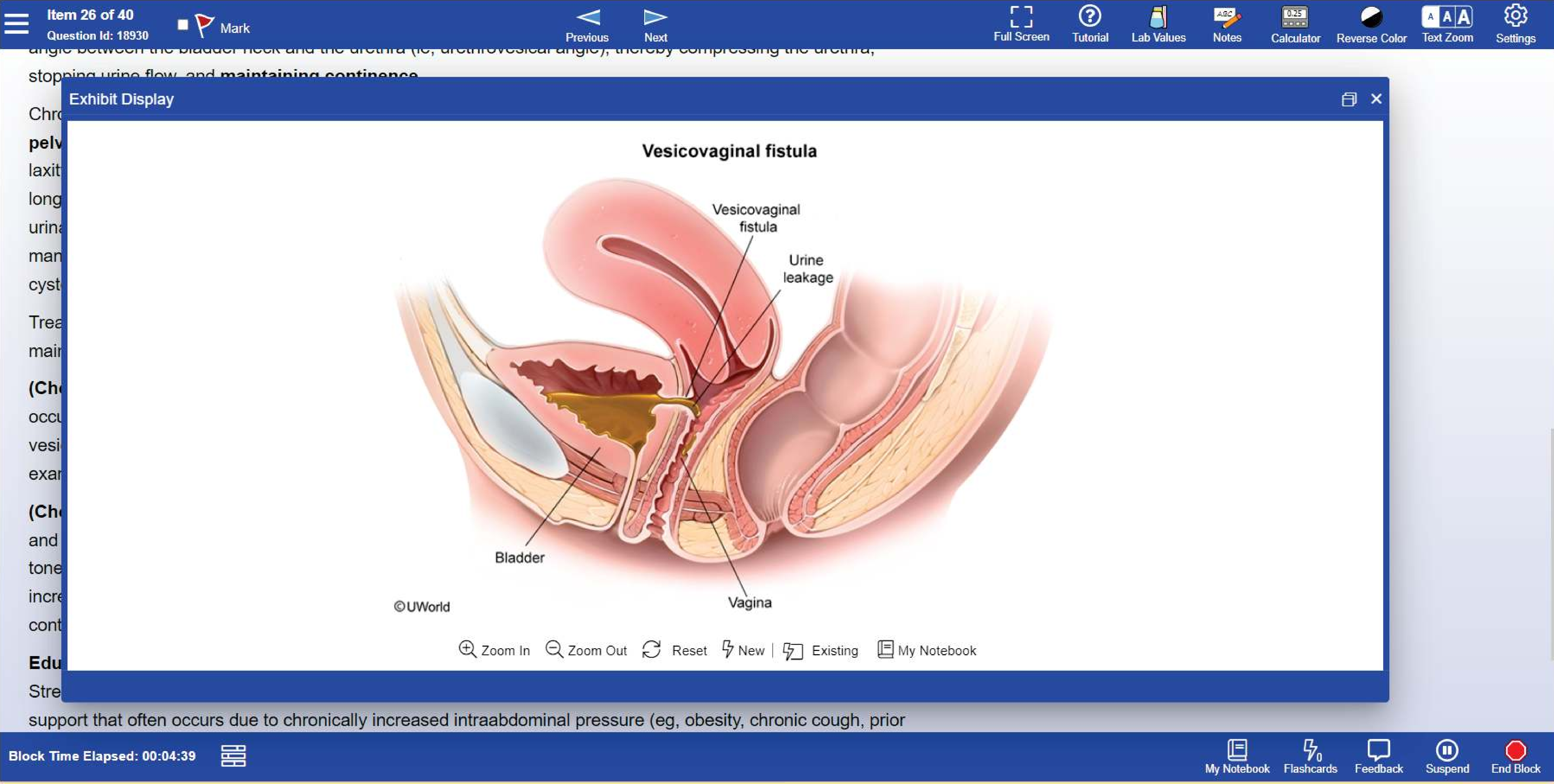
Educational objective:
Stress urinary incontinence (intermittent, involuntary leakage of urine) is caused by weakened pelvic floor muscle support that often occurs due to chronically increased intraabdominal pressure (eg, obesity, chronic cough, prior pregnancies).

References

- Diagnosis of urinary incontinence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angle between the bladder neck and the urethra (ie, urethrovesical angle), thereby compressing the urethra, stopping urine flow, and **maintaining continence**.

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Vesicovaginal fistula

Vesicovaginal fistula
Urine leakage
Bladder
Vagina

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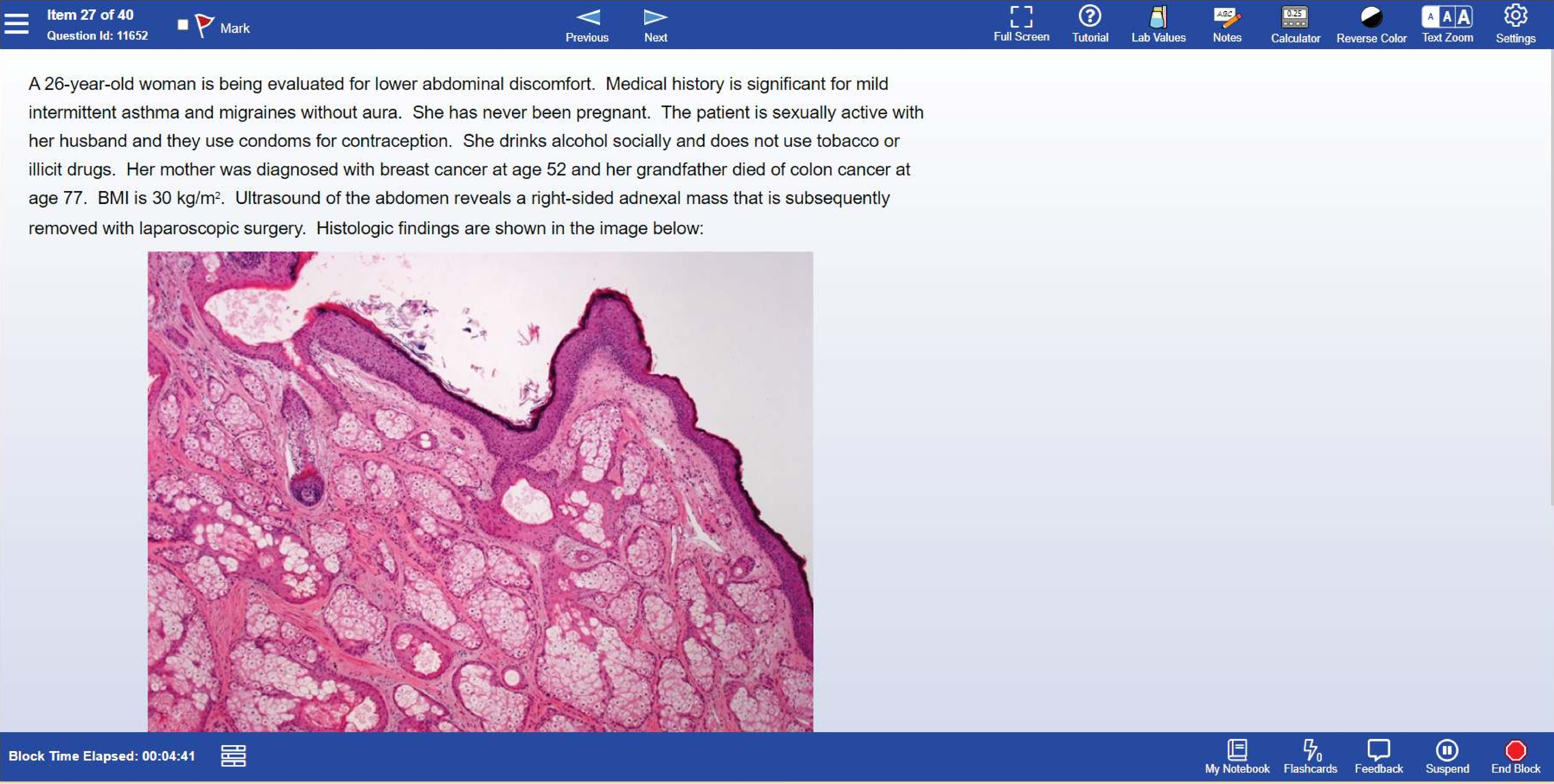

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A 26-year-old woman is being evaluated for lower abdominal discomfort. Medical history is significant for mild intermittent asthma and migraines without aura. She has never been pregnant. The patient is sexually active with her husband and they use condoms for contraception. She drinks alcohol socially and does not use tobacco or illicit drugs. Her mother was diagnosed with breast cancer at age 52 and her grandfather died of colon cancer at age 77. BMI is 30 kg/m^2. Ultrasound of the abdomen reveals a right-sided adnexal mass that is subsequently removed with laparoscopic surgery. Histologic findings are shown in the image below:

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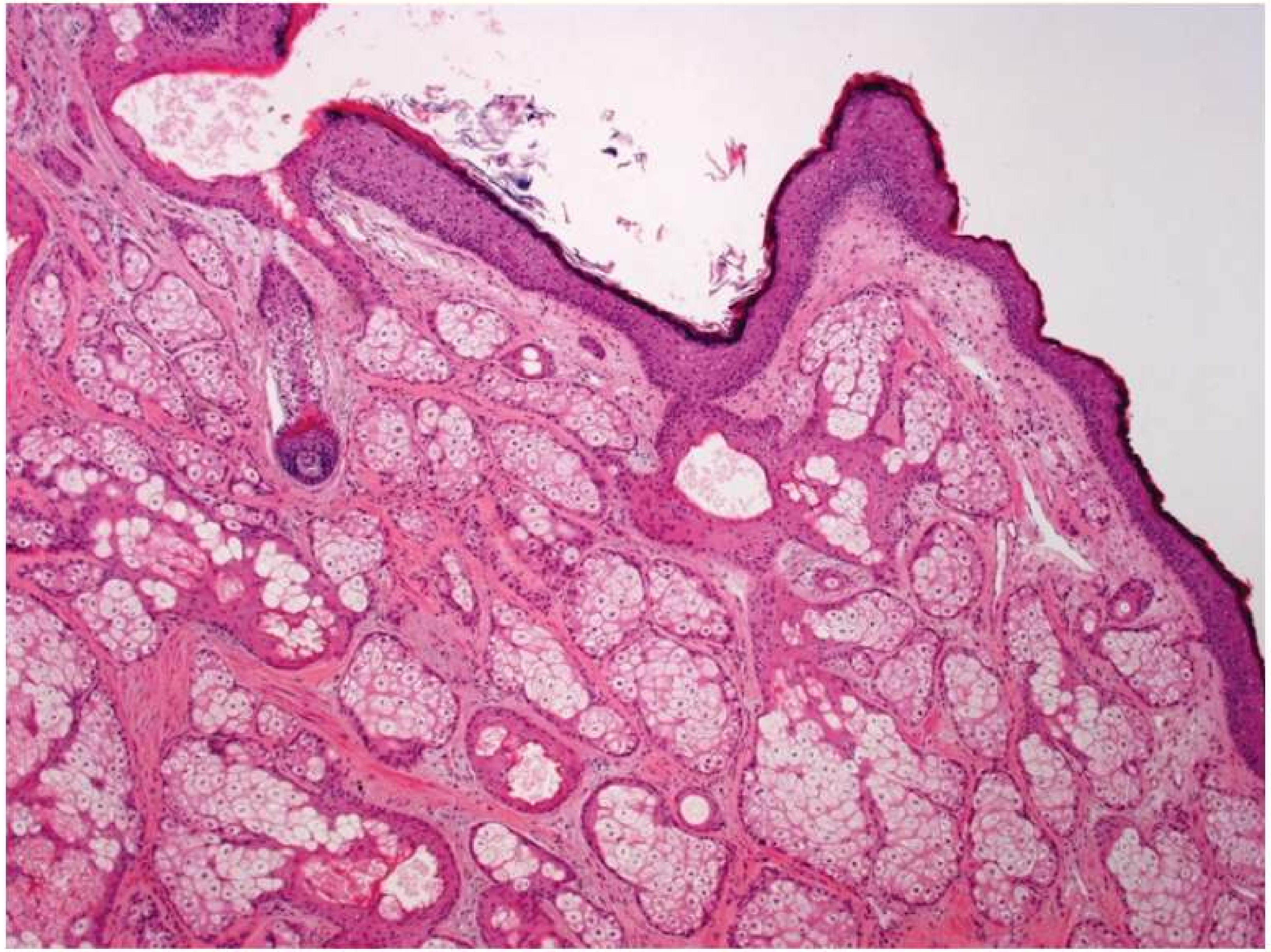

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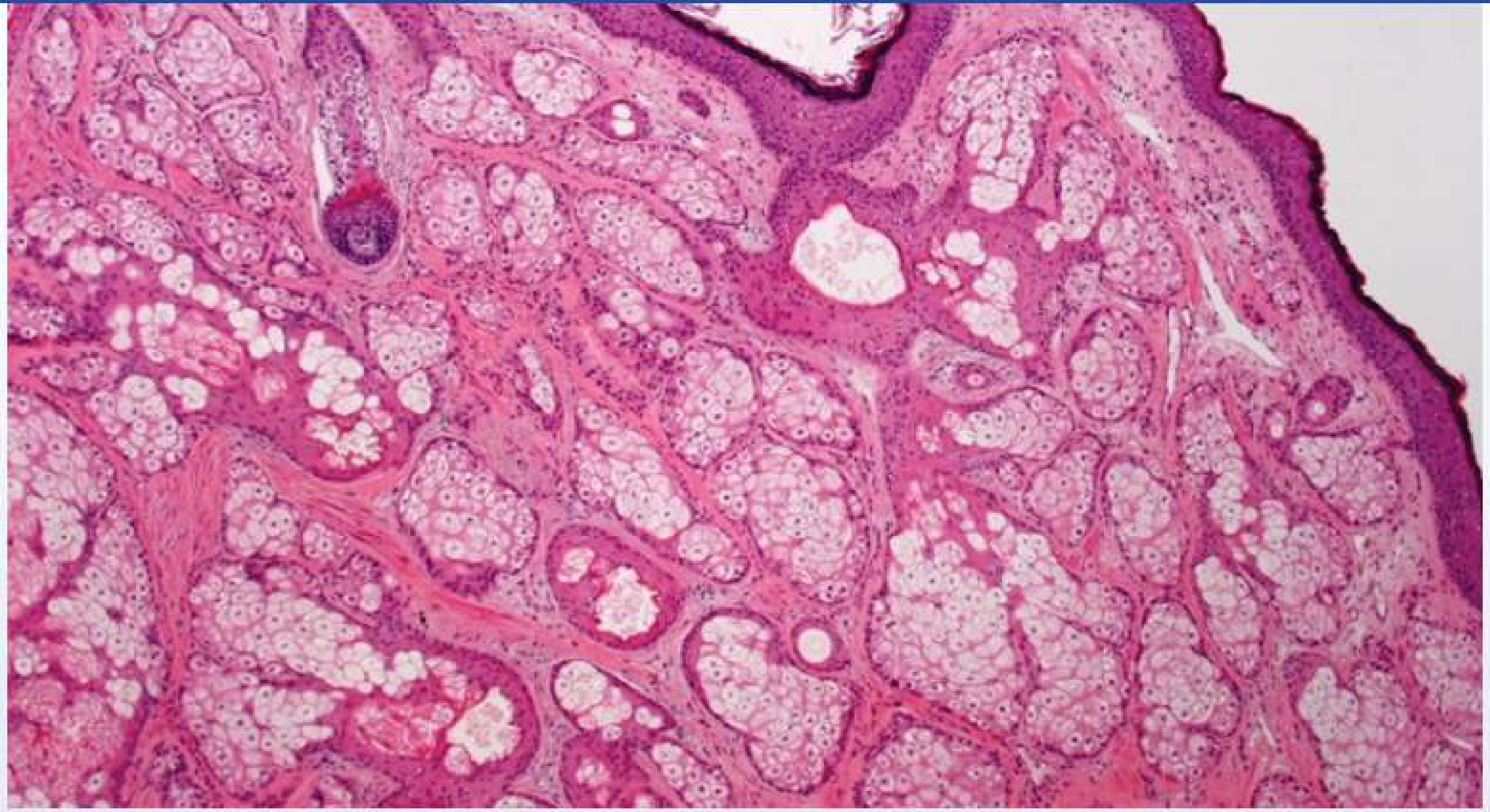

Which of the following is the most likely diagnosis?

- ○ A. Ectopic pregnancy
- ○ B. Endometriosis
- ○ C. High-grade serous ovarian carcinoma
- ○ D. Mature teratoma
- ○ E. Polycystic ovary syndrome

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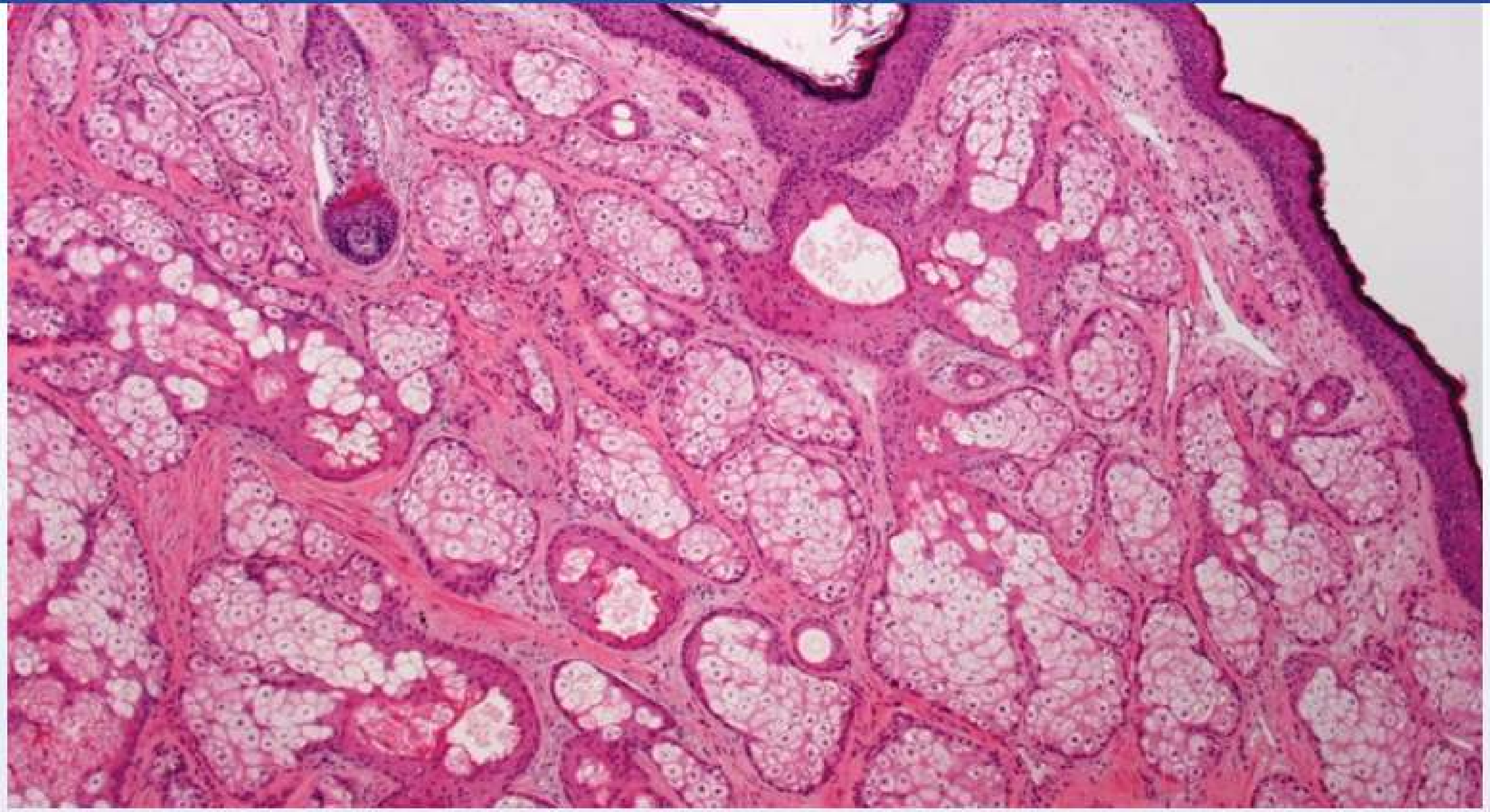

Which of the following is the most likely diagnosis?

- ○ A. Ectopic pregnancy (3%)
- ○ B. Endometriosis (13%)
- ○ C. High-grade serous ovarian carcinoma (34%)
- ✓ ○ D. Mature teratoma (38%)
- ✗ ● E. Polycystic ovary syndrome (10%)

Incorrect
Correct answer
D

38%
Answered correctly

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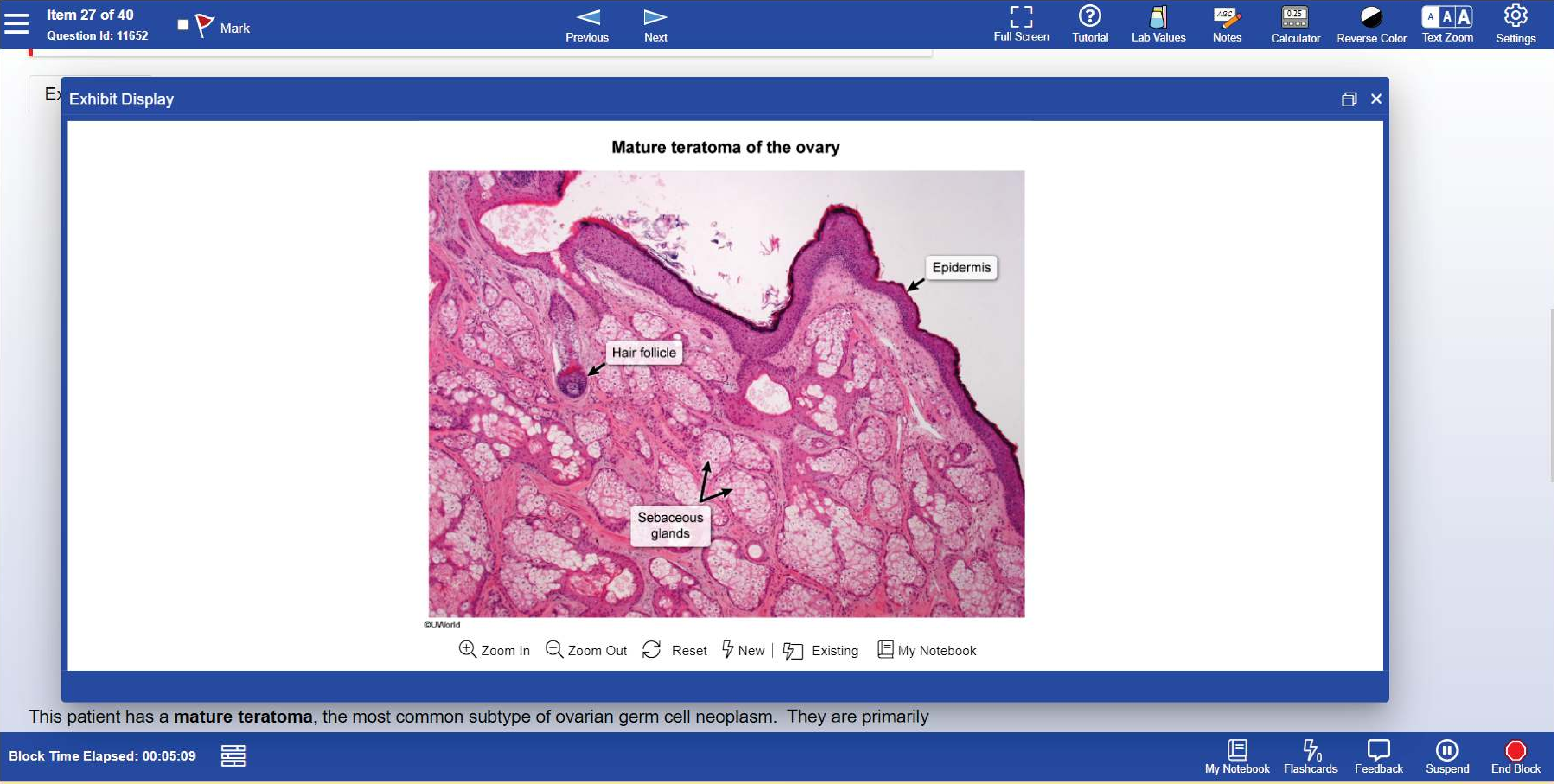
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Mature teratoma of the ovary

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This patient has a **mature teratoma**, the most common subtype of ovarian germ cell neoplasm. They are primarily

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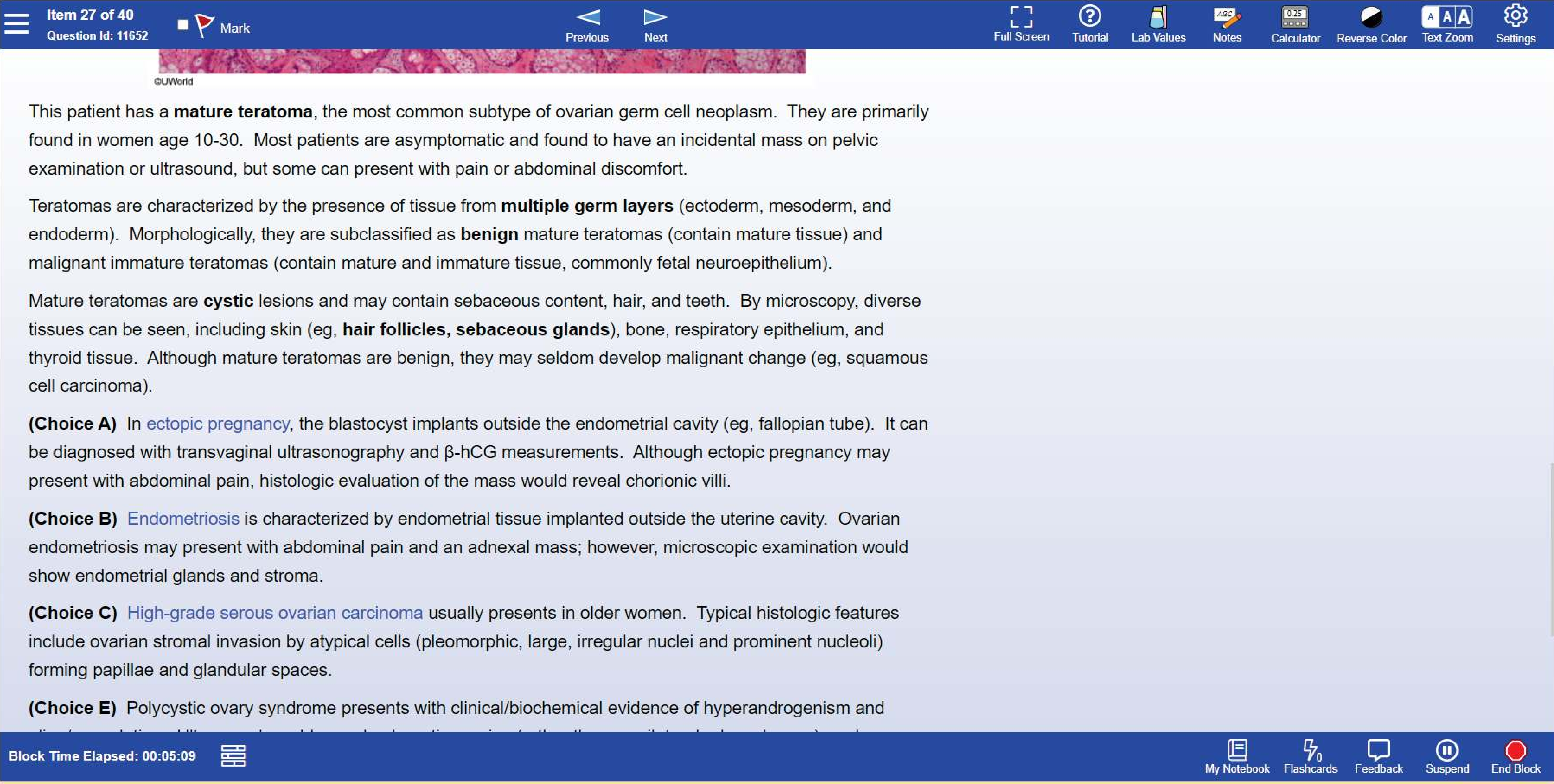
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This patient has a **mature teratoma**, the most common subtype of ovarian germ cell neoplasm. They are primarily found in women age 10-30. Most patients are asymptomatic and found to have an incidental mass on pelvic examination or ultrasound, but some can present with pain or abdominal discomfort.

Teratomas are characterized by the presence of tissue from **multiple germ layers** (ectoderm, mesoderm, and endoderm). Morphologically, they are subclassified as **benign** mature teratomas (contain mature tissue) and malignant immature teratomas (contain mature and immature tissue, commonly fetal neuroepithelium).

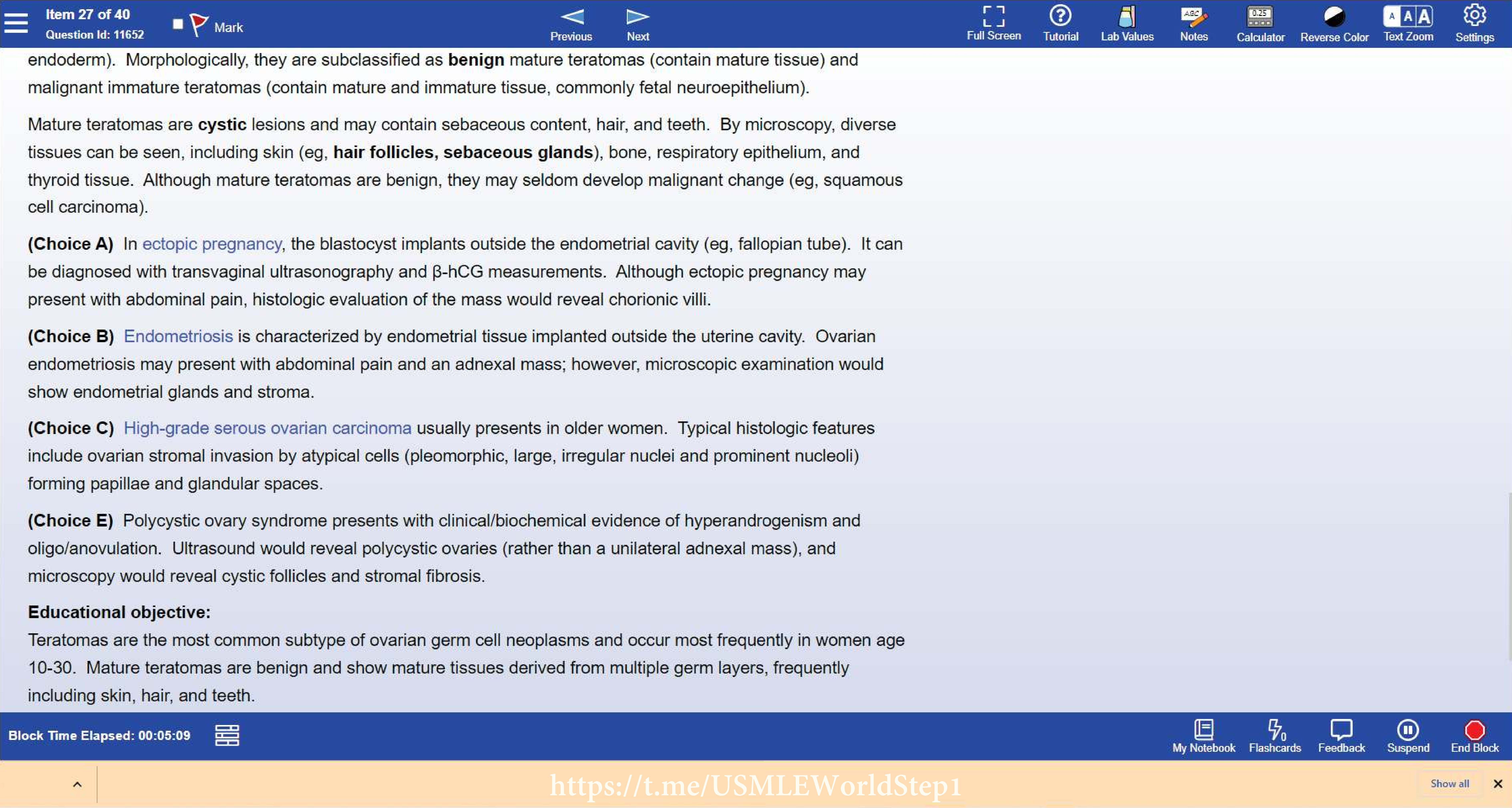
Mature teratomas are **cystic** lesions and may contain sebaceous content, hair, and teeth. By microscopy, diverse tissues can be seen, including skin (eg, **hair follicles, sebaceous glands**), bone, respiratory epithelium, and thyroid tissue. Although mature teratomas are benign, they may seldom develop malignant change (eg, squamous cell carcinoma).

(Choice A) In ectopic pregnancy, the blastocyst implants outside the endometrial cavity (eg, fallopian tube). It can be diagnosed with transvaginal ultrasonography and β-hCG measurements. Although ectopic pregnancy may present with abdominal pain, histologic evaluation of the mass would reveal chorionic villi.

(Choice B) Endometriosis is characterized by endometrial tissue implanted outside the uterine cavity. Ovarian endometriosis may present with abdominal pain and an adnexal mass; however, microscopic examination would show endometrial glands and stroma.

(Choice C) High-grade serous ovarian carcinoma usually presents in older women. Typical histologic features include ovarian stromal invasion by atypical cells (pleomorphic, large, irregular nuclei and prominent nucleoli) forming papillae and glandular spaces.

(Choice E) Polycystic ovary syndrome presents with clinical/biochemical evidence of hyperandrogenism and



endoderm). Morphologically, they are subclassified as **benign** mature teratomas (contain mature tissue) and malignant immature teratomas (contain mature and immature tissue, commonly fetal neuroepithelium).

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(Choice B) Endometriosis is characterized by endometrial tissue implanted outside the uterine cavity. Ovarian endometriosis may present with abdominal pain and an adnexal mass; however, microscopic examination would show endometrial glands and stroma.

(Choice C) High-grade serous ovarian carcinoma usually presents in older women. Typical histologic features include ovarian stromal invasion by atypical cells (pleomorphic, large, irregular nuclei and prominent nucleoli) forming papillae and glandular spaces.

(Choice E) Polycystic ovary syndrome presents with clinical/biochemical evidence of hyperandrogenism and oligo/anovulation. Ultrasound would reveal polycystic ovaries (rather than a unilateral adnexal mass), and microscopy would reveal cystic follicles and stromal fibrosis.

Educational objective:
Teratomas are the most common subtype of ovarian germ cell neoplasms and occur most frequently in women age 10-30. Mature teratomas are benign and show mature tissues derived from multiple germ layers, frequently including skin, hair, and teeth.

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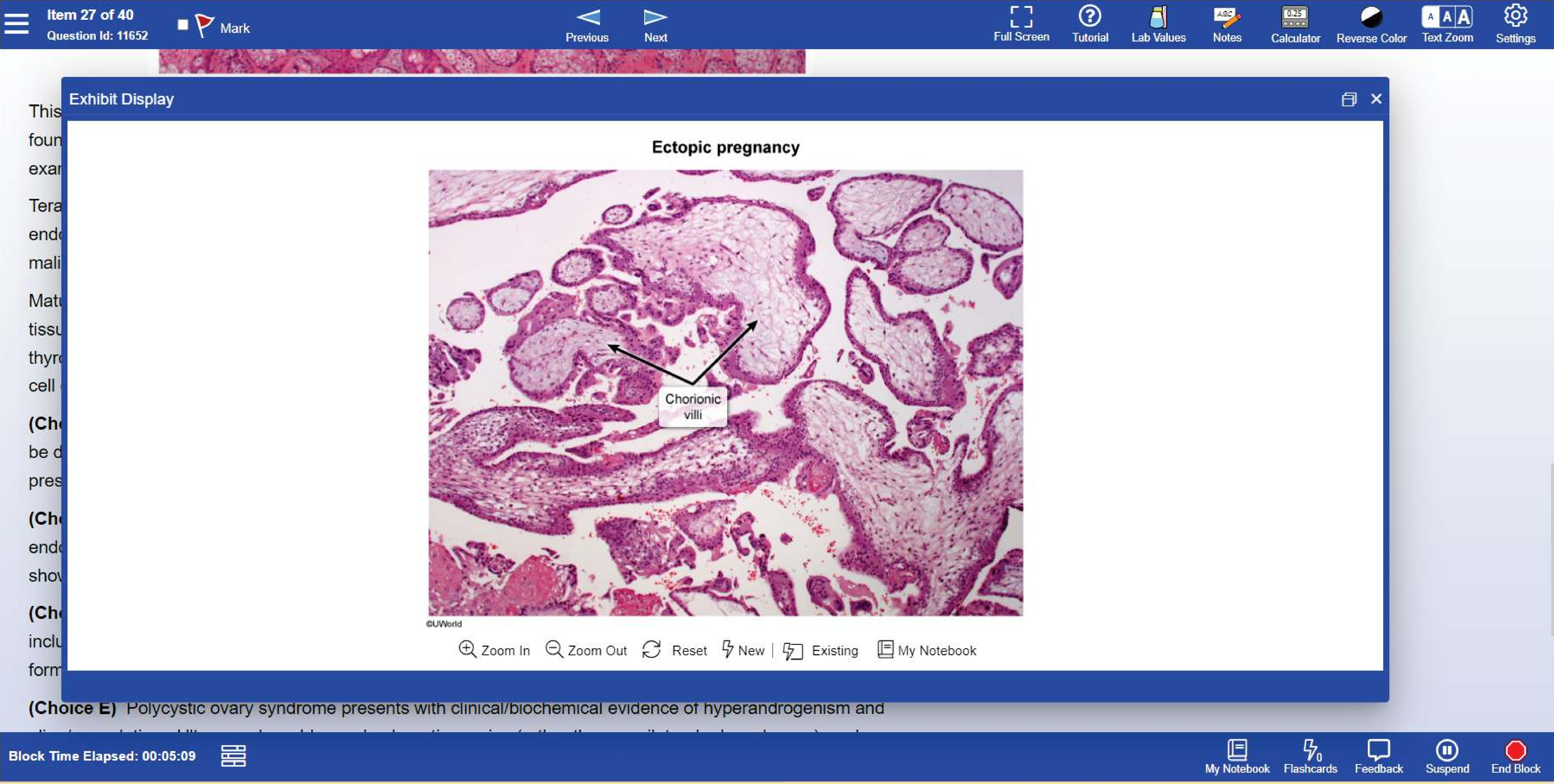
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Ectopic pregnancy

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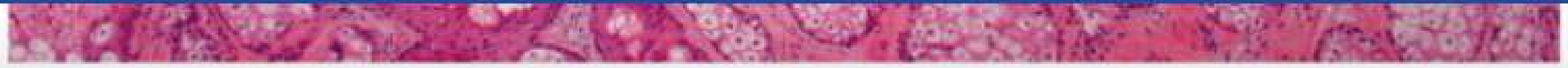
(Choice E) Polycystic ovary syndrome presents with clinical/biochemical evidence of hyperandrogenism and



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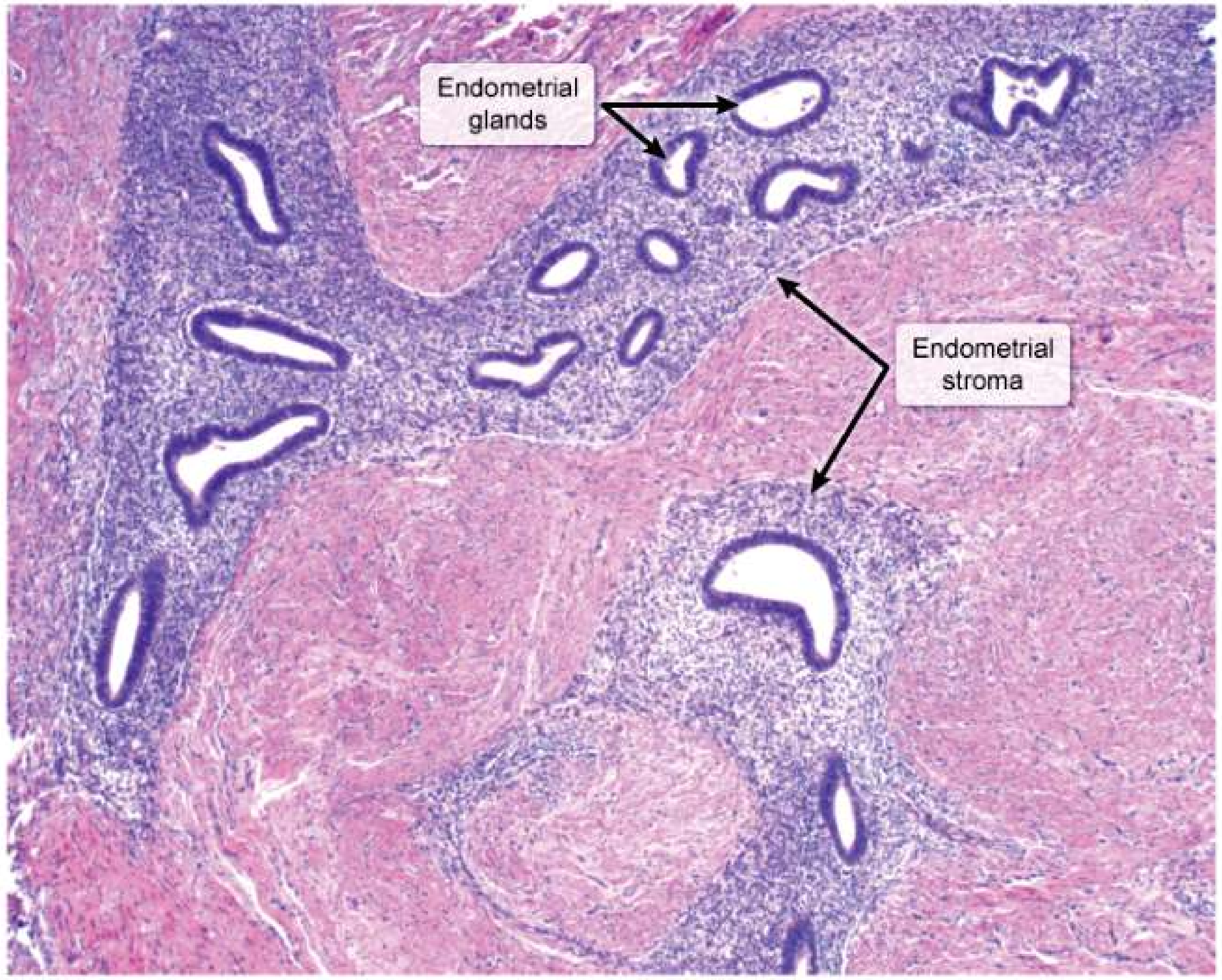
Endometriosis



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(Choice E) Polycystic ovary syndrome presents with clinical/biochemical evidence of hyperandrogenism and

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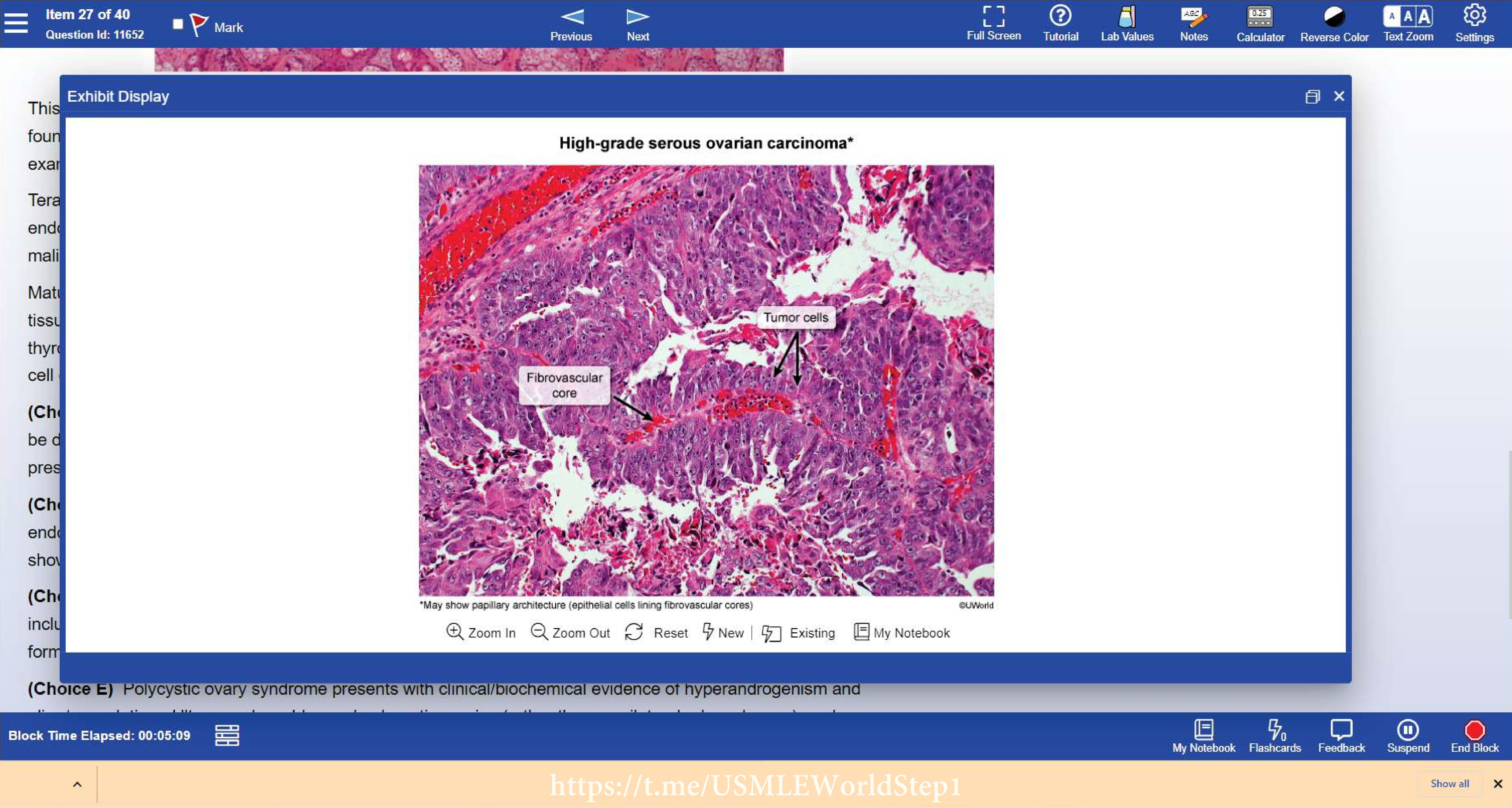
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Fibrovascular core
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High-grade serous ovarian carcinoma*

*May show papillary architecture (epithelial cells lining fibrovascular cores)

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(Choice E) Polycystic ovary syndrome presents with clinical/biochemical evidence of hyperandrogenism and

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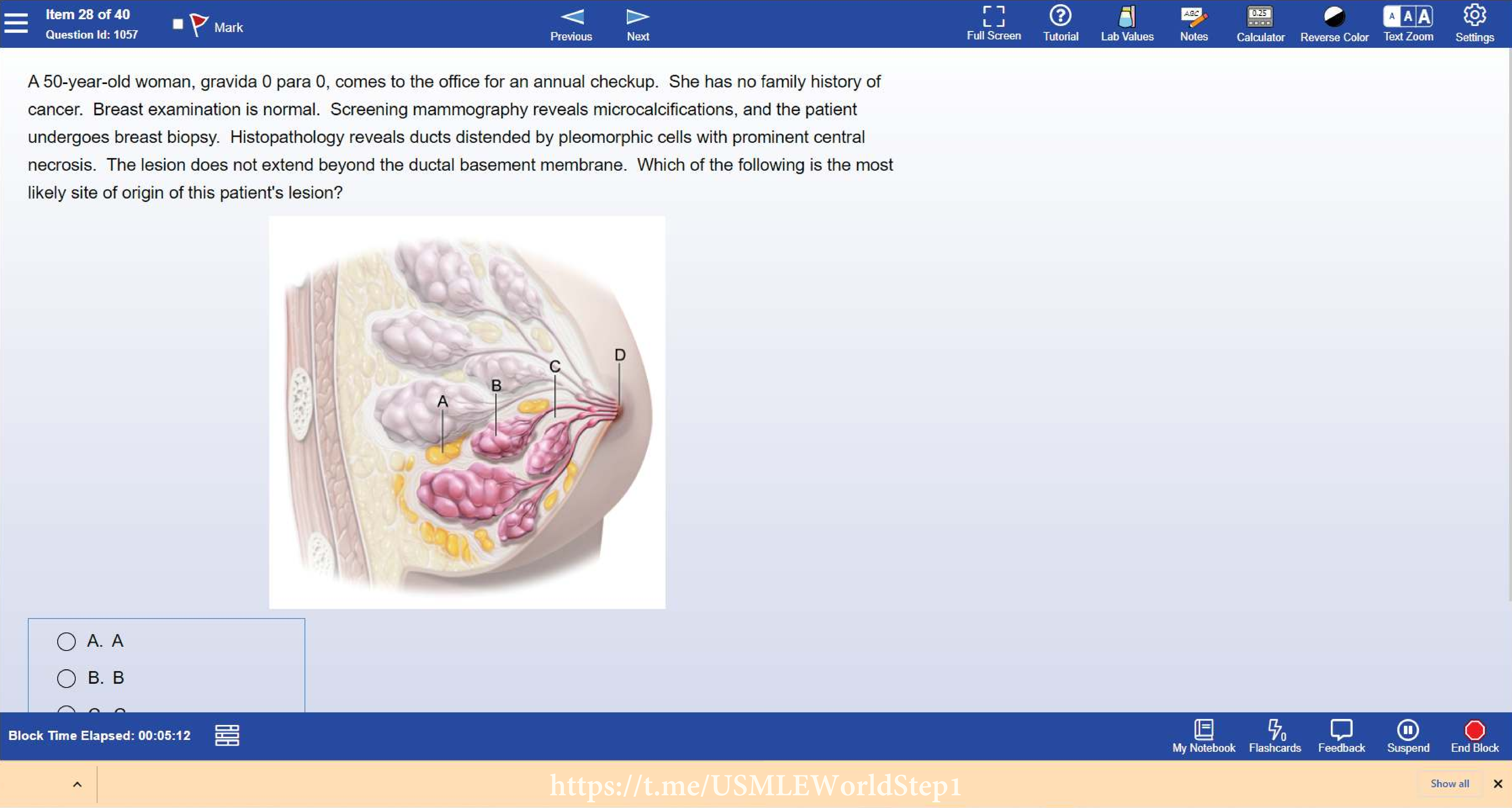
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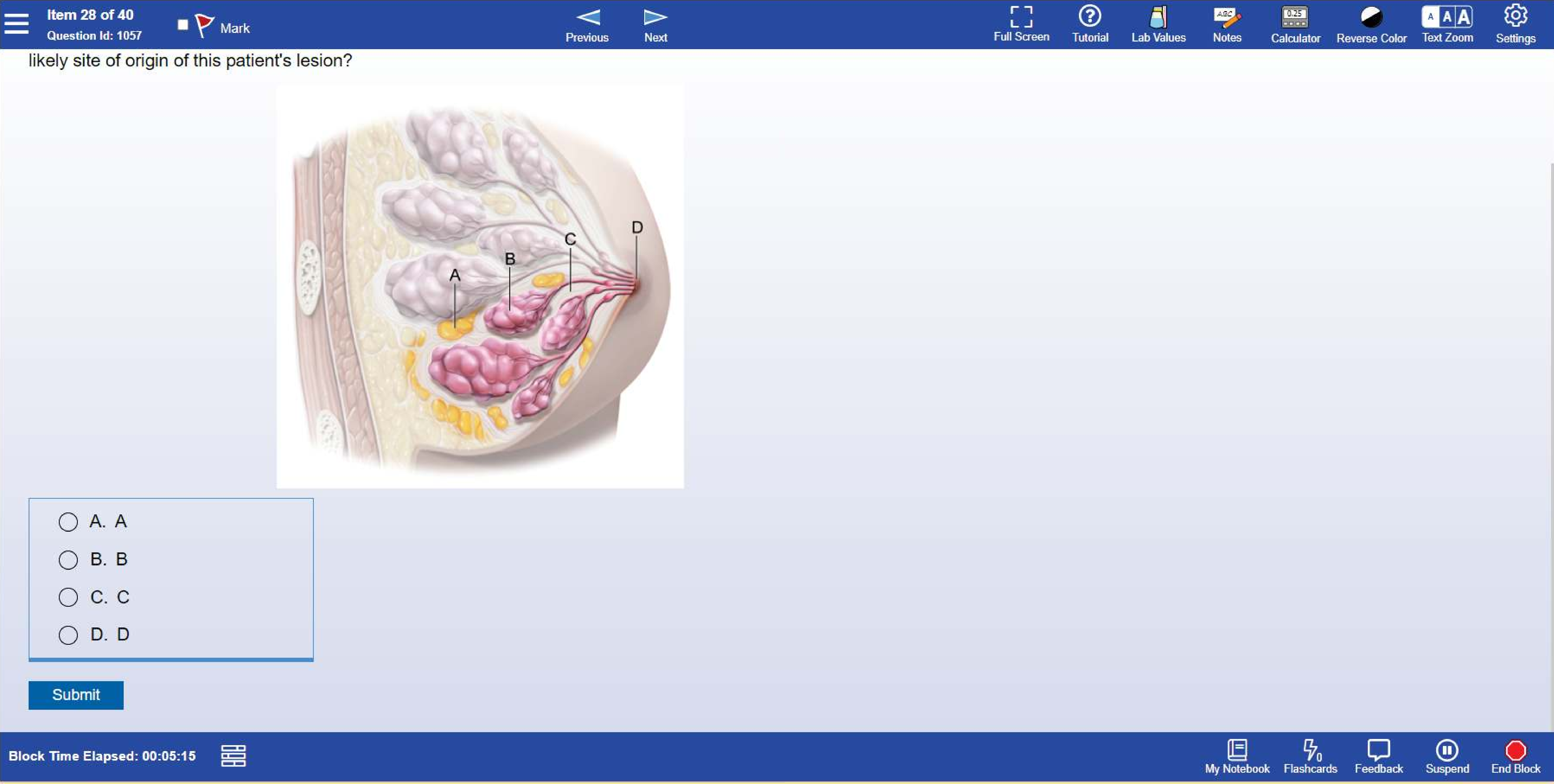
A 50-year-old woman, gravida 0 para 0, comes to the office for an annual checkup. She has no family history of cancer. Breast examination is normal. Screening mammography reveals microcalcifications, and the patient undergoes breast biopsy. Histopathology reveals ducts distended by pleomorphic cells with prominent central necrosis. The lesion does not extend beyond the ductal basement membrane. Which of the following is the most likely site of origin of this patient's lesion?

○ A. A

○ B. B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likely site of origin of this patient's lesion?

○ A. A

○ B. B

○ C. C

○ D. D

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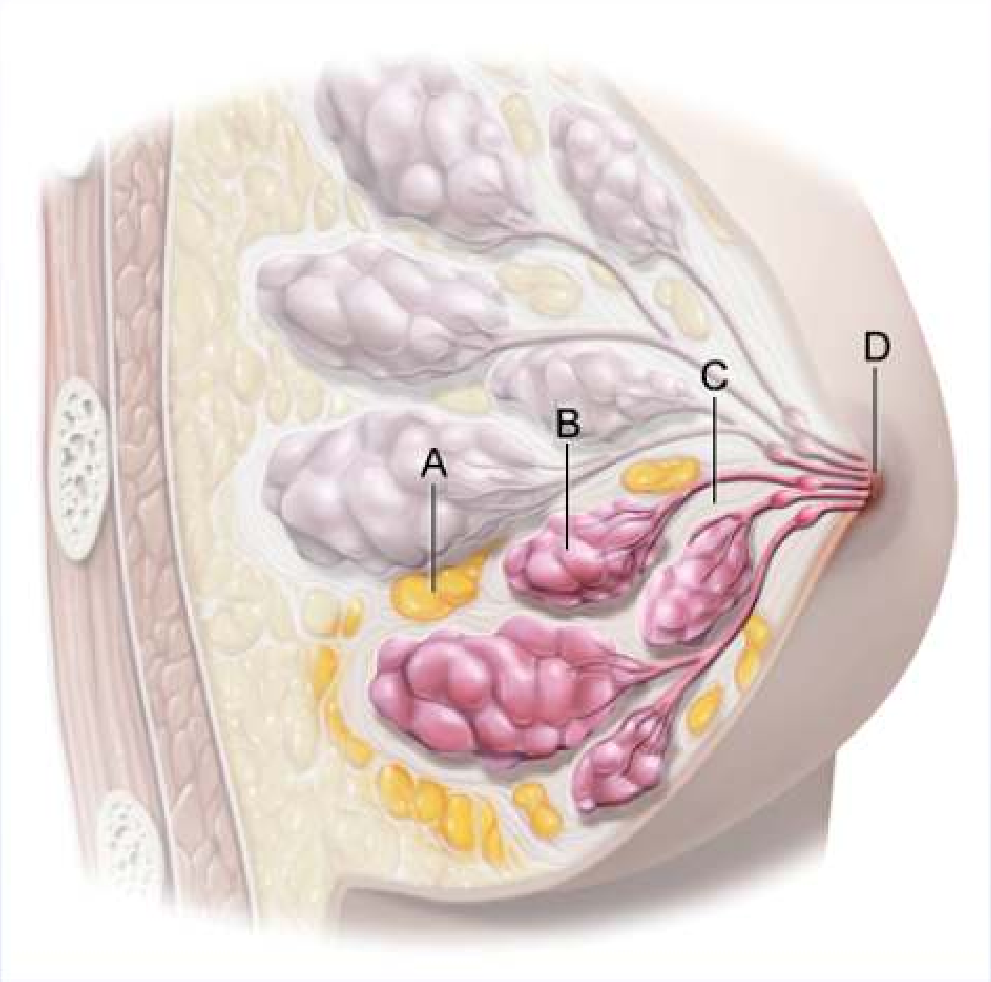
likely site of origin of this patient's lesion?



○ A. A (6%)

✓ ○ B. B (64%)

✗ ● C. C (13%)

○ D. D (15%)

Incorrect
Correct answer
B

64%
Answered correctly

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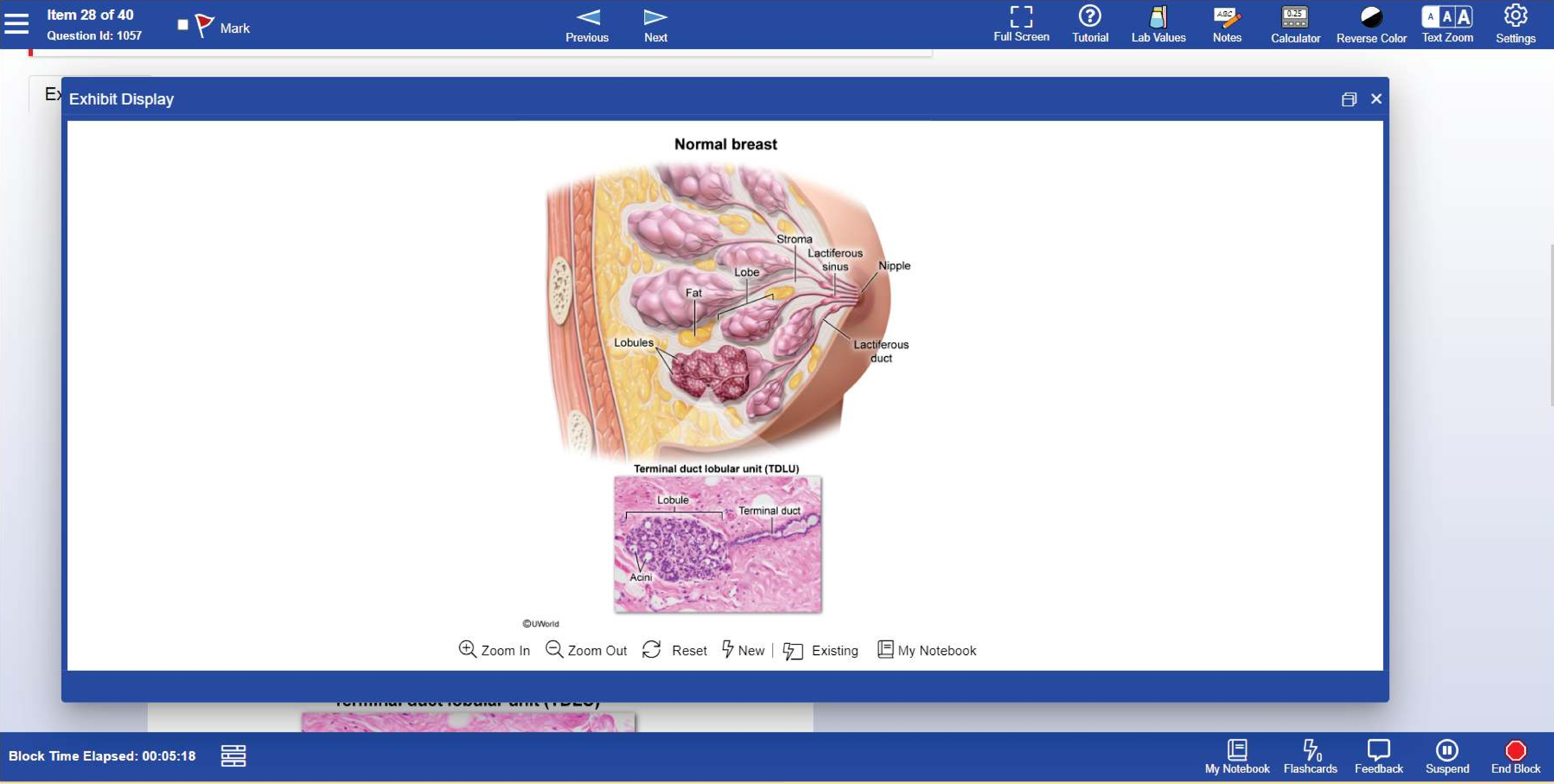
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Exhibit Display

Normal breast

Stroma
Lactiferous sinus
Nipple
Lobe
Fat
Lobules
Lactiferous duct

Terminal duct lobular unit (TDLU)

Lobule
Terminal duct
Acini
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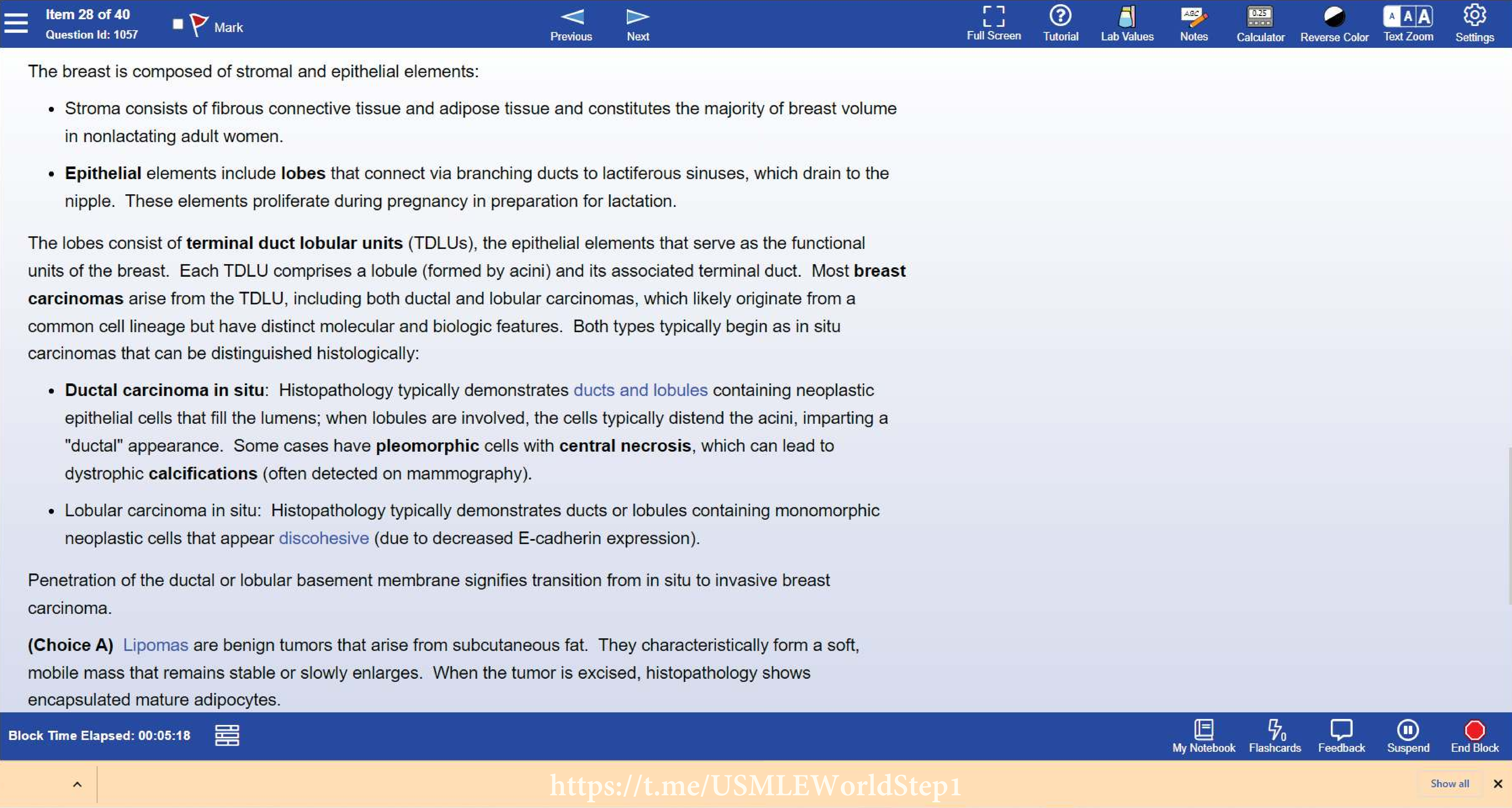
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The breast is composed of stromal and epithelial elements:

- Stroma consists of fibrous connective tissue and adipose tissue and constitutes the majority of breast volume in nonlactating adult women.
- **Epithelial** elements include **lobes** that connect via branching ducts to lactiferous sinuses, which drain to the nipple. These elements proliferate during pregnancy in preparation for lactation.

The lobes consist of **terminal duct lobular units** (TDLUs), the epithelial elements that serve as the functional units of the breast. Each TDLU comprises a lobule (formed by acini) and its associated terminal duct. Most **breast carcinomas** arise from the TDLU, including both ductal and lobular carcinomas, which likely originate from a common cell lineage but have distinct molecular and biologic features. Both types typically begin as in situ carcinomas that can be distinguished histologically:

- **Ductal carcinoma in situ**: Histopathology typically demonstrates ducts and lobules containing neoplastic epithelial cells that fill the lumens; when lobules are involved, the cells typically distend the acini, imparting a "ductal" appearance. Some cases have **pleomorphic** cells with **central necrosis**, which can lead to dystrophic **calcifications** (often detected on mammography).
- Lobular carcinoma in situ: Histopathology typically demonstrates ducts or lobules containing monomorphic neoplastic cells that appear discohesive (due to decreased E-cadherin expression).

Penetration of the ductal or lobular basement membrane signifies transition from in situ to invasive breast carcinoma.

(Choice A) Lipomas are benign tumors that arise from subcutaneous fat. They characteristically form a soft, mobile mass that remains stable or slowly enlarges. When the tumor is excised, histopathology shows encapsulated mature adipocytes.

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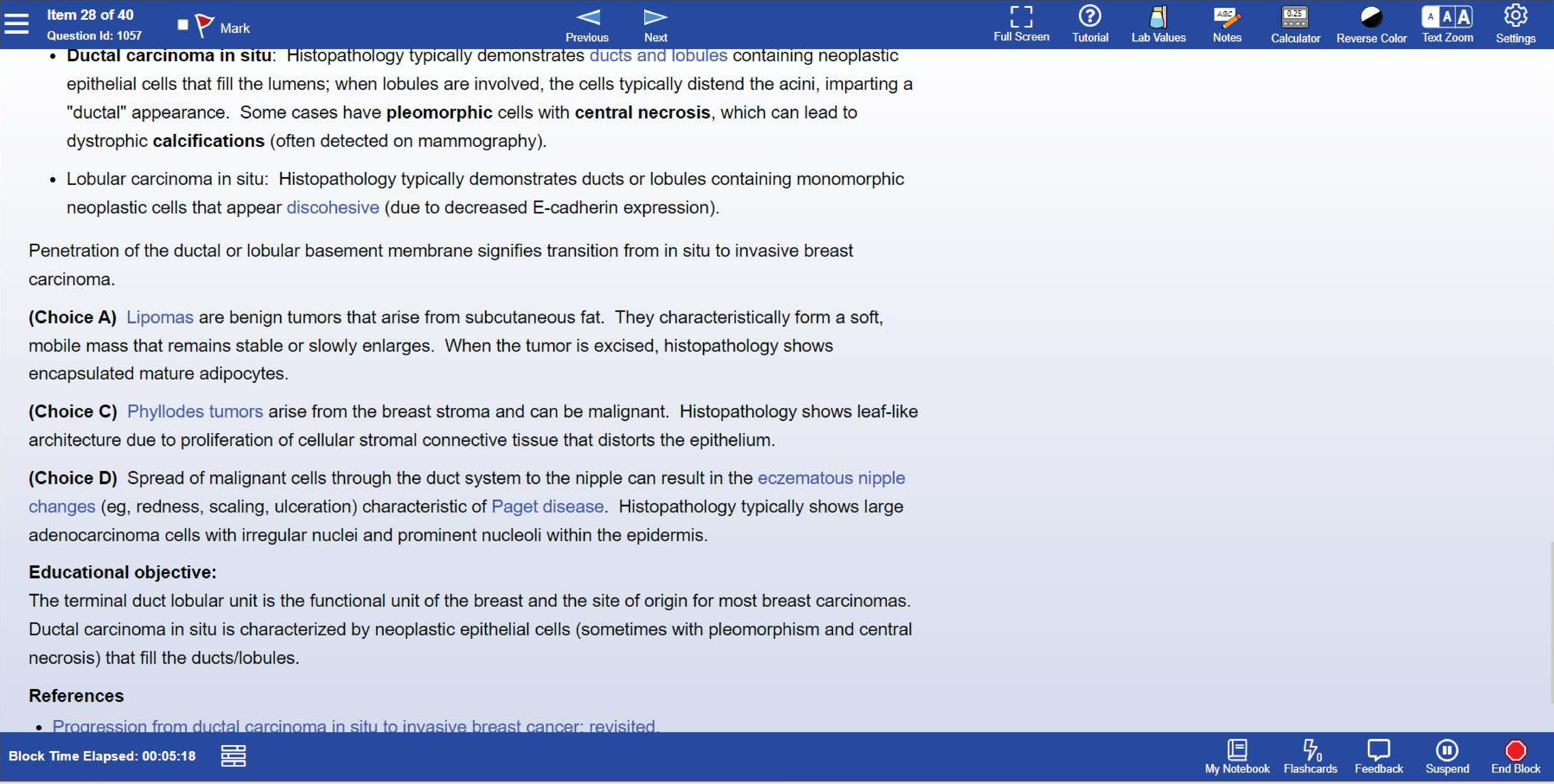
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(Choice A) Lipomas are benign tumors that arise from subcutaneous fat. They characteristically form a soft, mobile mass that remains stable or slowly enlarges. When the tumor is excised, histopathology shows encapsulated mature adipocytes.

(Choice C) Phyllodes tumors arise from the breast stroma and can be malignant. Histopathology shows leaf-like architecture due to proliferation of cellular stromal connective tissue that distorts the epithelium.

(Choice D) Spread of malignant cells through the duct system to the nipple can result in the eczematous nipple changes (eg, redness, scaling, ulceration) characteristic of Paget disease. Histopathology typically shows large adenocarcinoma cells with irregular nuclei and prominent nucleoli within the epidermis.

Educational objective:

The terminal duct lobular unit is the functional unit of the breast and the site of origin for most breast carcinomas. Ductal carcinoma in situ is characterized by neoplastic epithelial cells (sometimes with pleomorphism and central necrosis) that fill the ducts/lobules.

References

- Progression from ductal carcinoma in situ to invasive breast cancer: revisited.

The lobes consist of **terminal duct lobular units** (TDLUs), the epithelial elements that serve as the functional

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adenocarcinoma cells with irregular nuclei and prominent nucleoli within the epidermis.

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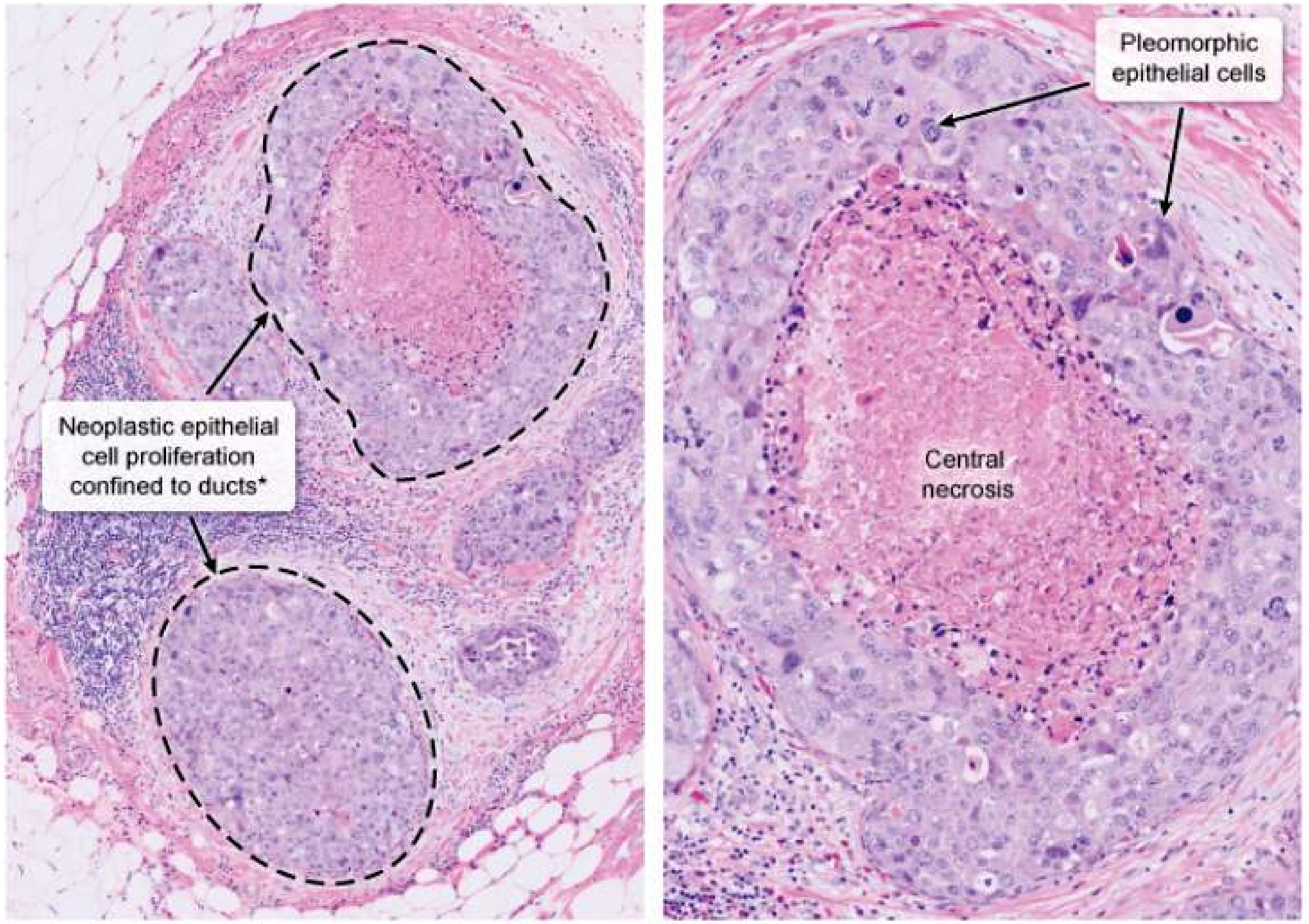
Ductal carcinoma in situ


Neoplastic epithelial cell proliferation confined to ducts*
Pleomorphic epithelial cells
Central necrosis

*Does not invade basement membrane.

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The lobes consist of **terminal duct lobular units** (TDLUs), the epithelial elements that serve as the functional

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adenocarcinoma cells with irregular nuclei and prominent nucleoli within the epidermis.

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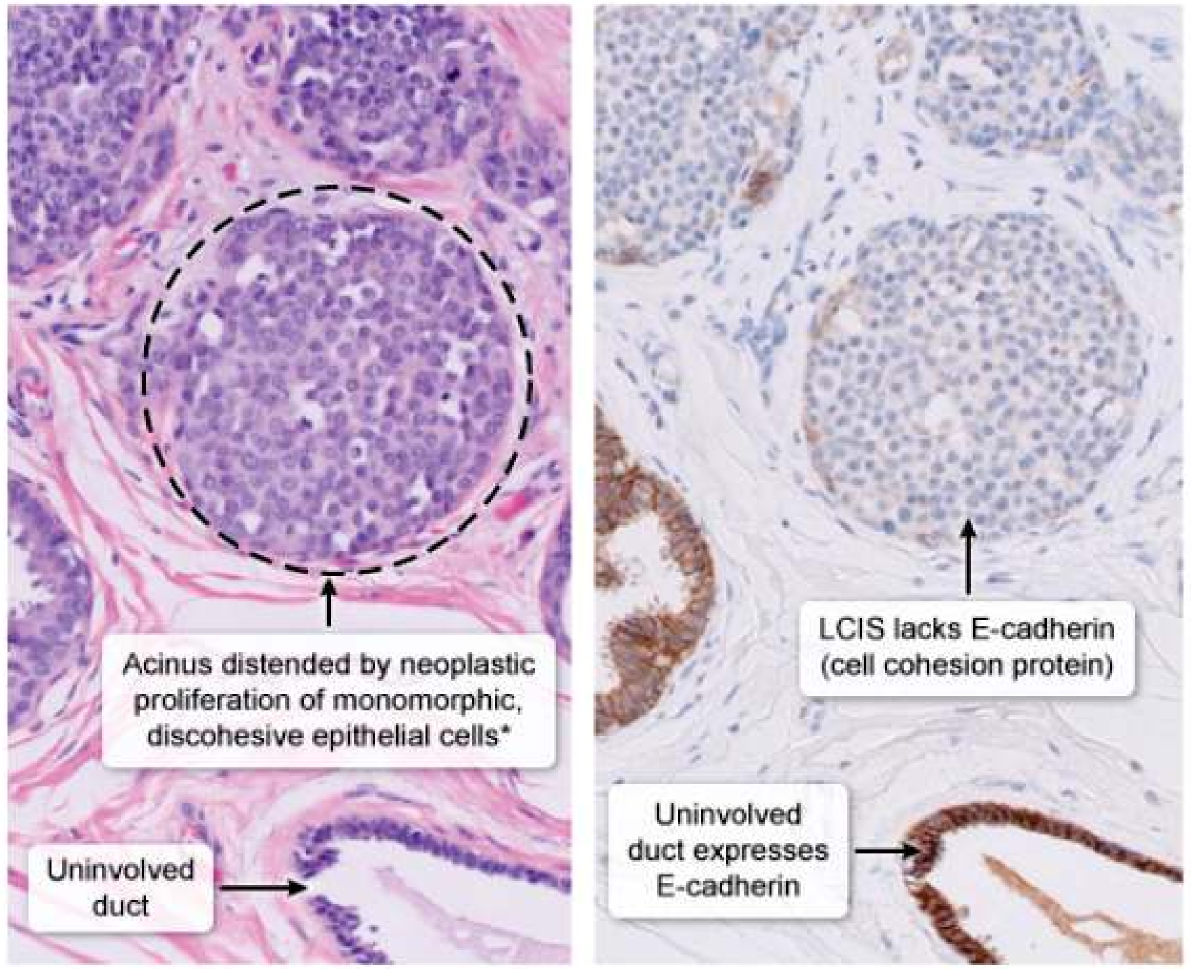
Lobular carcinoma in situ


Acinus distended by neoplastic proliferation of monomorphic, discohesive epithelial cells*
Uninvolved duct
LCIS lacks E-cadherin (cell cohesion protein)
Uninvolved duct expresses E-cadherin

Hematoxylin & eosin stain

E-cadherin immunohistochemical stain

*Do not invade basement membrane.
LCIS = lobular carcinoma in situ.

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The lobes consist of **terminal duct lobular units** (TDLUs), the epithelial elements that serve as the functional

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adenocarcinoma cells with irregular nuclei and prominent nucleoli within the epidermis.

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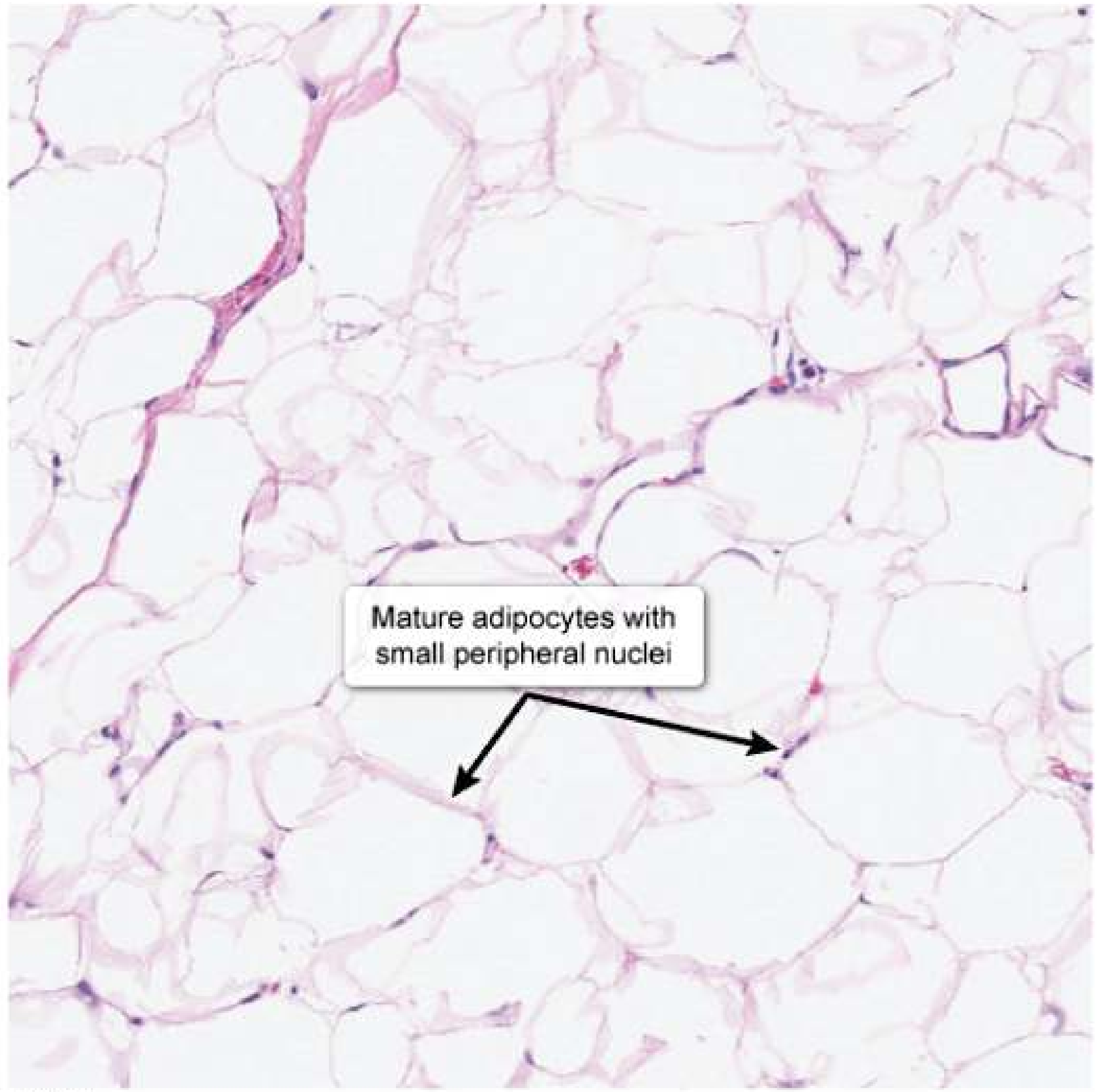
Lipoma



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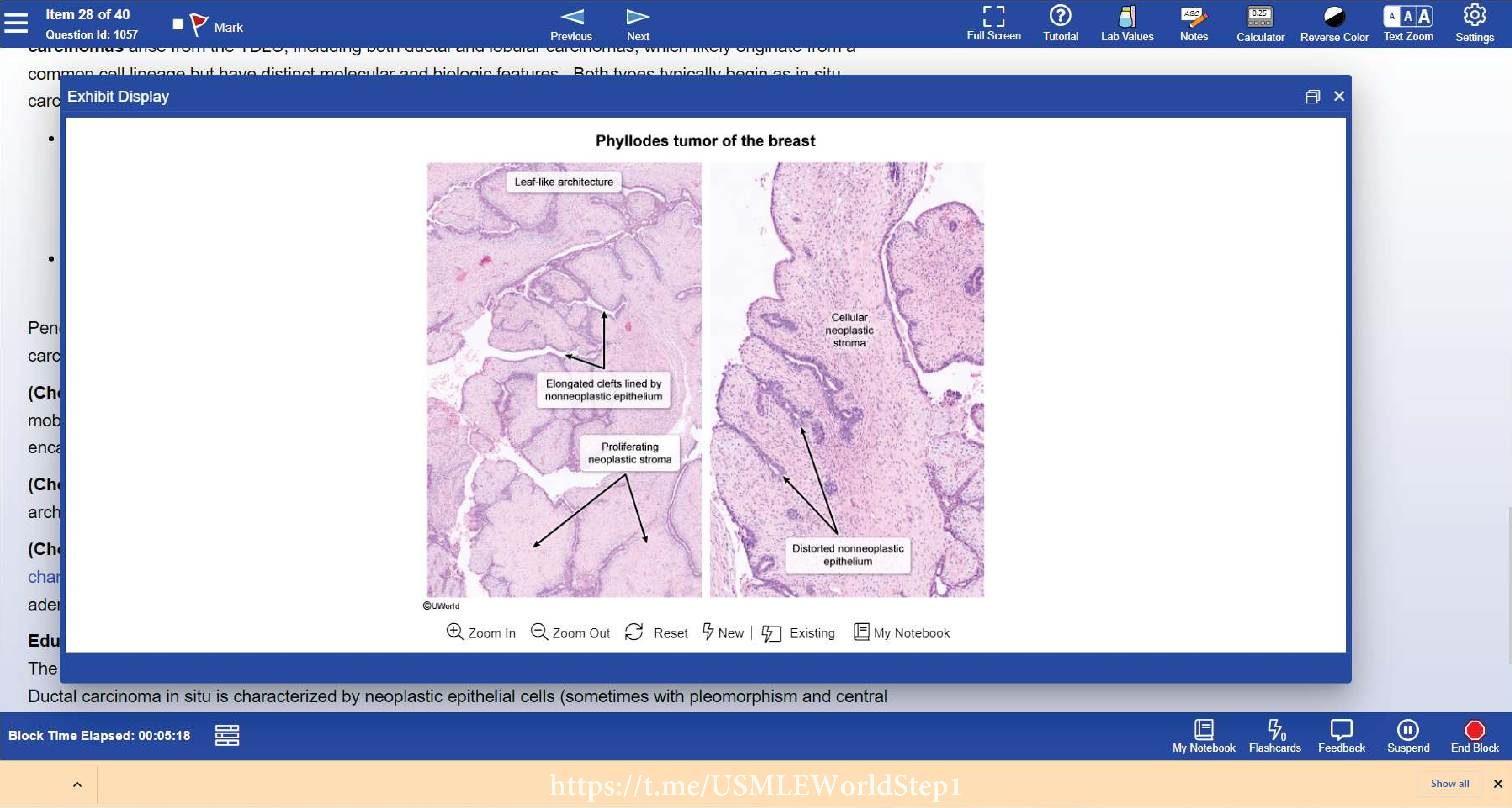
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carcinomas arise from the TDLU, including both ductal and lobular carcinomas, which likely originate from a common cell lineage but have distinct molecular and biologic features. Both types typically begin as in situ carc

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Ductal carcinoma in situ is characterized by neoplastic epithelial cells (sometimes with pleomorphism and central

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Phyllodes tumor of the breast

Leaf-like architecture
Elongated clefts lined by nonneoplastic epithelium
Proliferating neoplastic stroma
Cellular neoplastic stroma
Distorted nonneoplastic epithelium
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carcinomas arise from the TDLU, including both ductal and lobular carcinomas, which likely originate from a common cell lineage but have distinct molecular and biologic features. Both types typically begin as in situ carc

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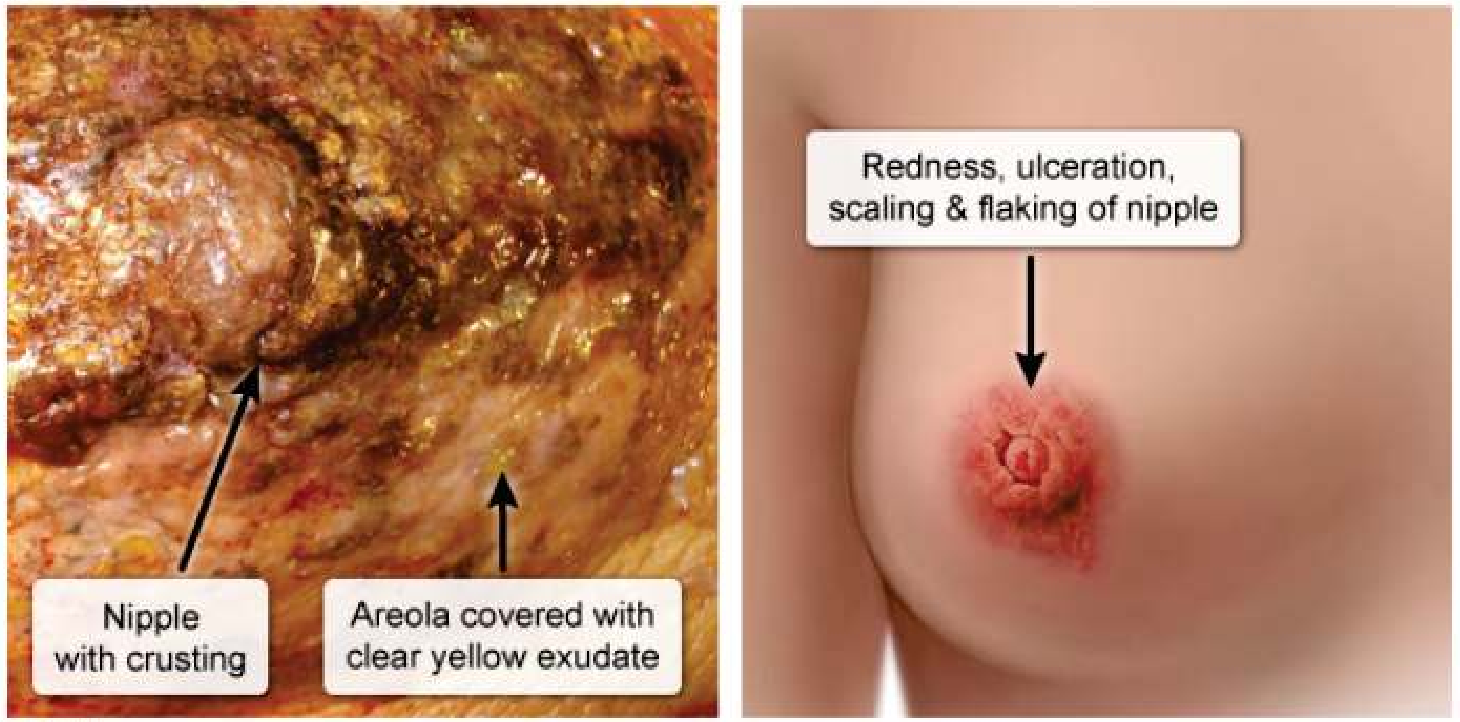
Paget disease of the breast


Nipple with crusting
Areola covered with clear yellow exudate
Redness, ulceration, scaling & flaking of nipple

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Ductal carcinoma in situ is characterized by neoplastic epithelial cells (sometimes with pleomorphism and central

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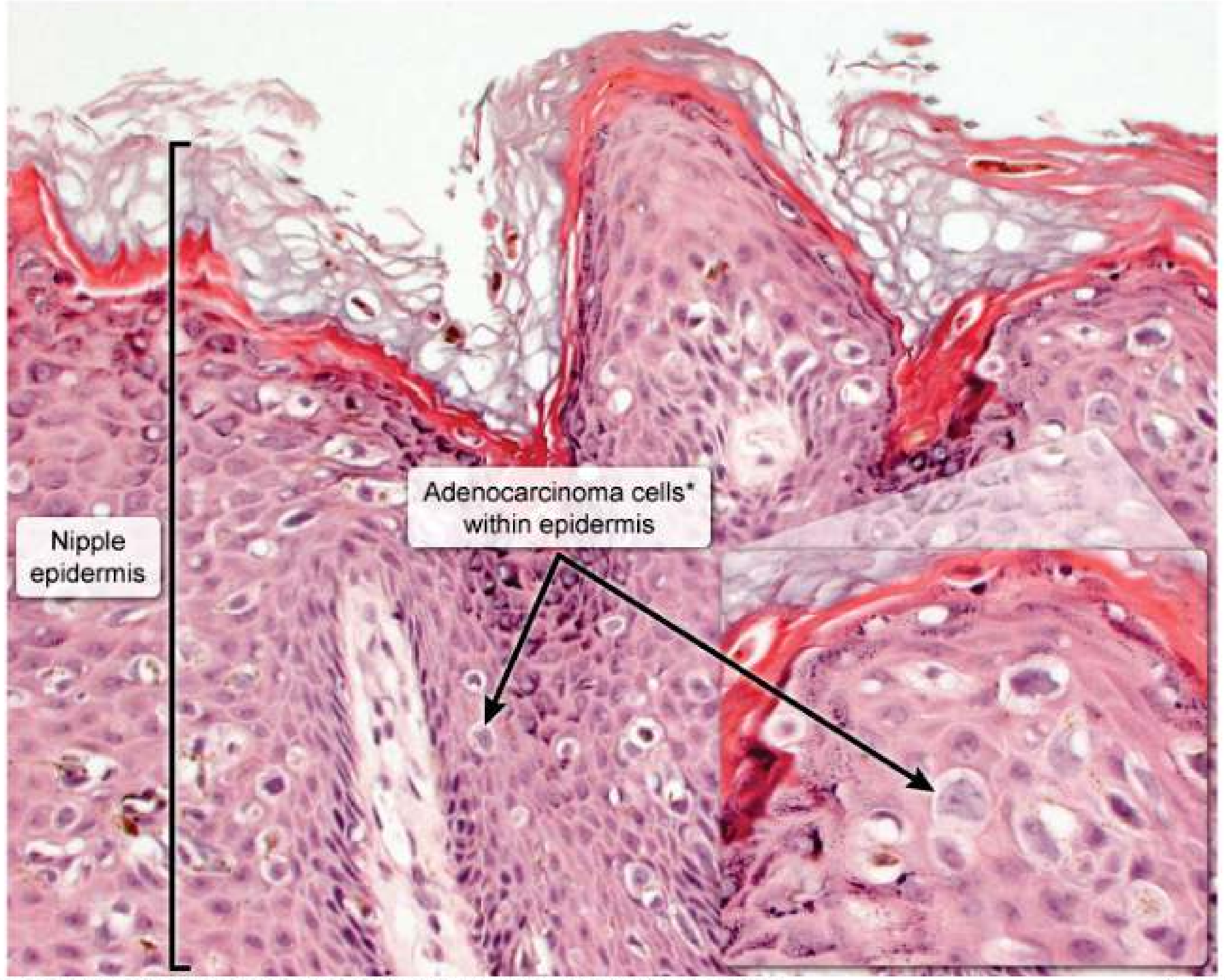
Paget disease of the breast


Nipple epidermis
Adenocarcinoma cells* within epidermis

*Large cells with abundant pale cytoplasm, irregular nuclei, and prominent nucleoli.

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Ductal carcinoma in situ is characterized by neoplastic epithelial cells (sometimes with pleomorphism and central

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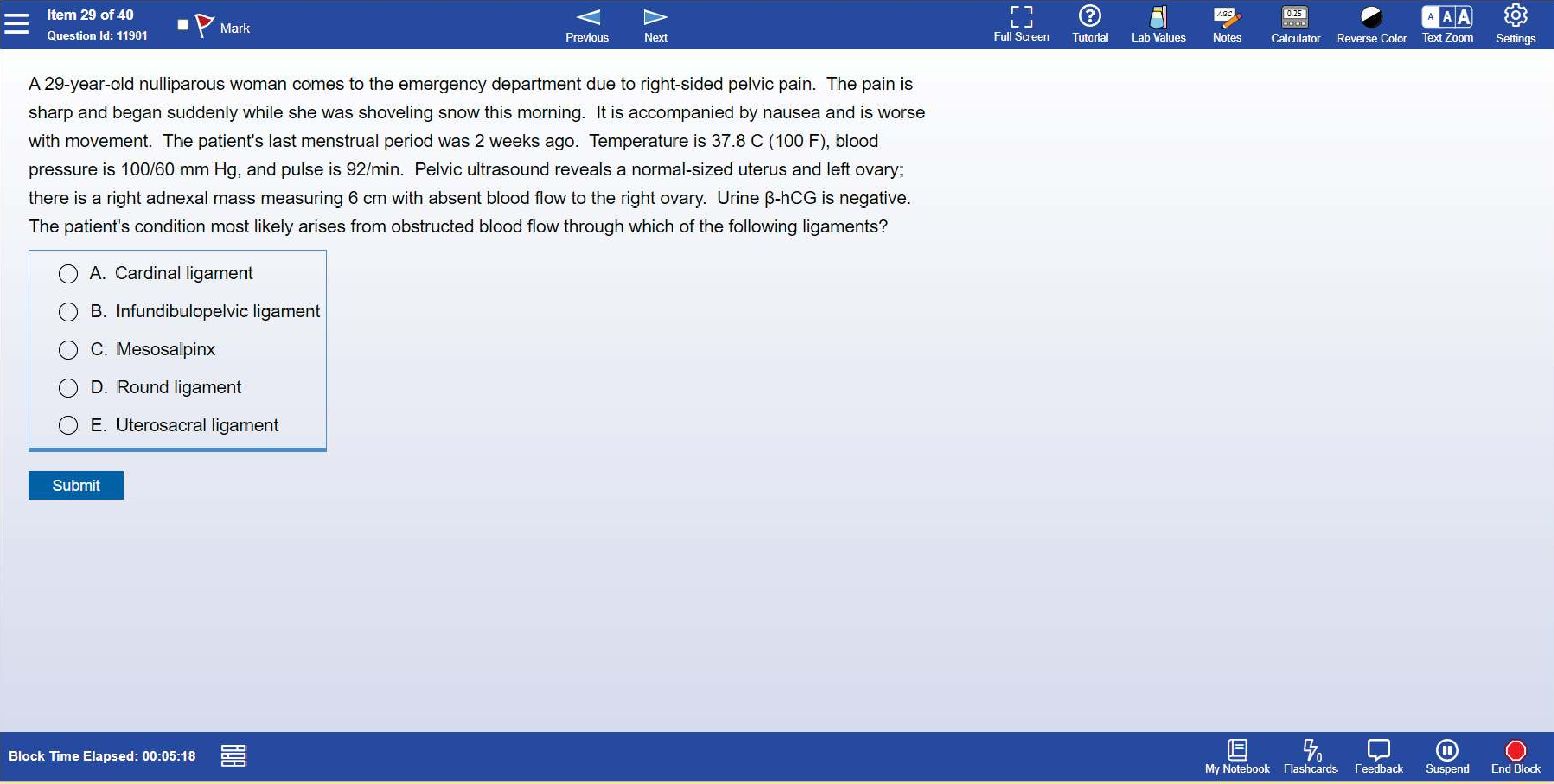
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A 29-year-old nulliparous woman comes to the emergency department due to right-sided pelvic pain. The pain is sharp and began suddenly while she was shoveling snow this morning. It is accompanied by nausea and is worse with movement. The patient's last menstrual period was 2 weeks ago. Temperature is 37.8 C (100 F), blood pressure is 100/60 mm Hg, and pulse is 92/min. Pelvic ultrasound reveals a normal-sized uterus and left ovary; there is a right adnexal mass measuring 6 cm with absent blood flow to the right ovary. Urine β-hCG is negative. The patient's condition most likely arises from obstructed blood flow through which of the following ligaments?

○ A. Cardinal ligament
○ B. Infundibulopelvic ligament
○ C. Mesosalpinx
○ D. Round ligament
○ E. Uterosacral ligament

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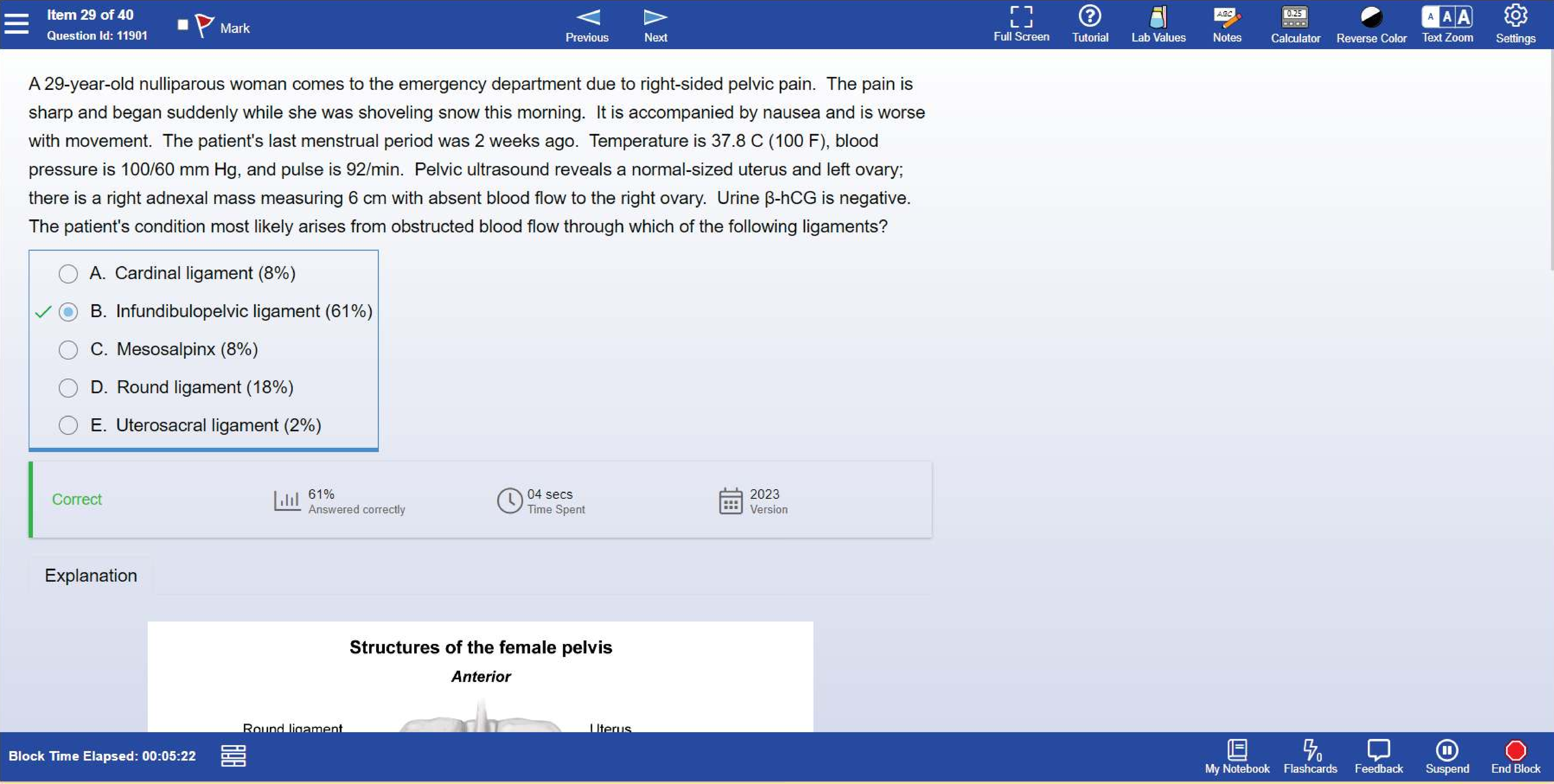
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A 29-year-old nulliparous woman comes to the emergency department due to right-sided pelvic pain. The pain is sharp and began suddenly while she was shoveling snow this morning. It is accompanied by nausea and is worse with movement. The patient's last menstrual period was 2 weeks ago. Temperature is 37.8 C (100 F), blood pressure is 100/60 mm Hg, and pulse is 92/min. Pelvic ultrasound reveals a normal-sized uterus and left ovary; there is a right adnexal mass measuring 6 cm with absent blood flow to the right ovary. Urine β-hCG is negative. The patient's condition most likely arises from obstructed blood flow through which of the following ligaments?

- ○ A. Cardinal ligament (8%)
- ✓ ● B. Infundibulopelvic ligament (61%)
- ○ C. Mesosalpinx (8%)
- ○ D. Round ligament (18%)
- ○ E. Uterosacral ligament (2%)

Correct

61% Answered correctly

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Explanation

Structures of the female pelvis

Anterior

Round ligament
Uterus
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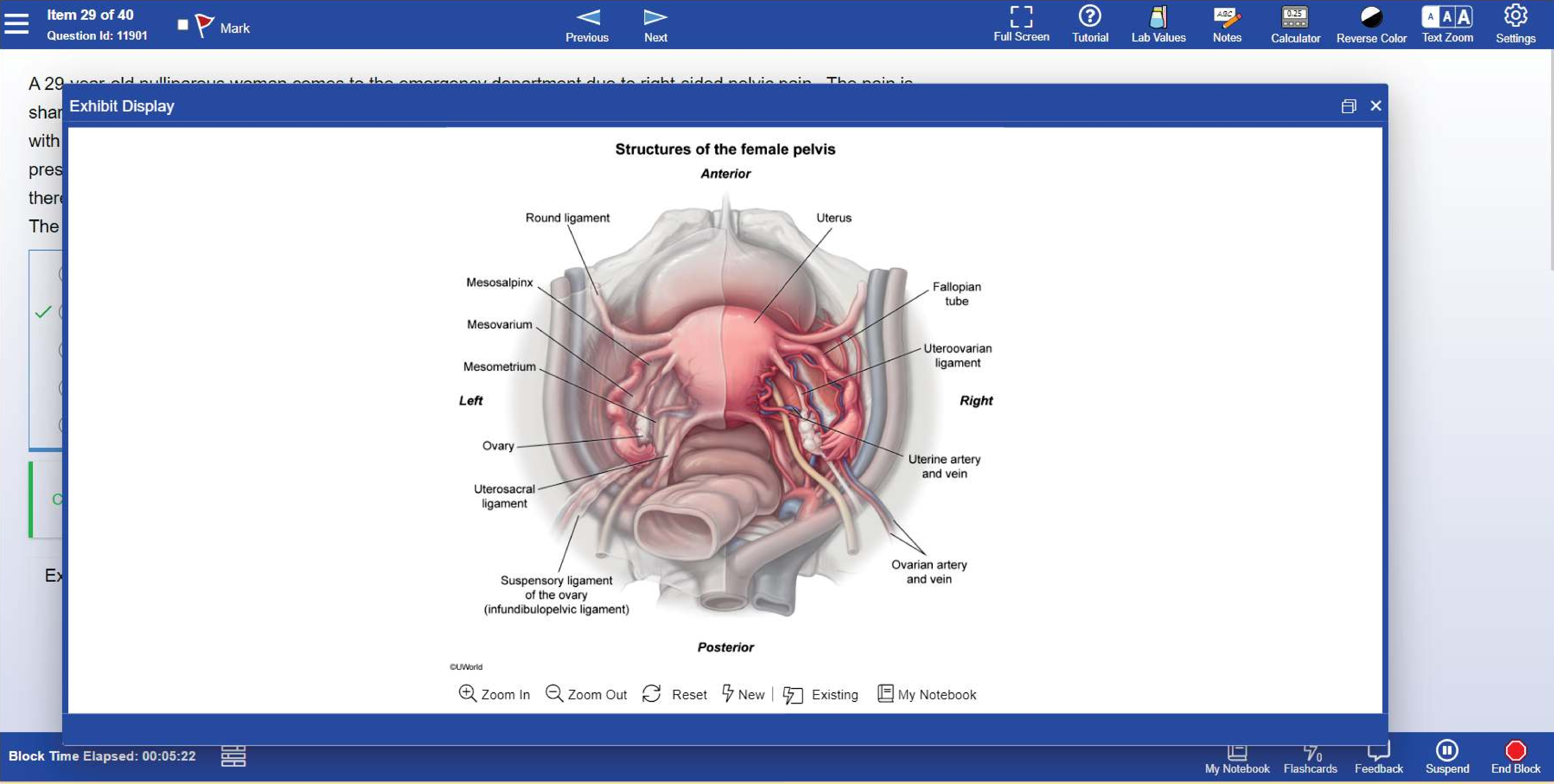
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A 29-year-old nulliparous woman comes to the emergency department due to right-sided pelvic pain. The pain is

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Exhibit Display

Structures of the female pelvis

Anterior
Round ligament
Uterus
Mesosalpinx
Fallopian tube
Mesovarium
Uteroovarian ligament
Mesometrium
Left
Right
Ovary
Uterine artery and vein
Uterosacral ligament
Ovarian artery and vein
Suspensory ligament of the ovary (infundibulopelvic ligament)
Posterior

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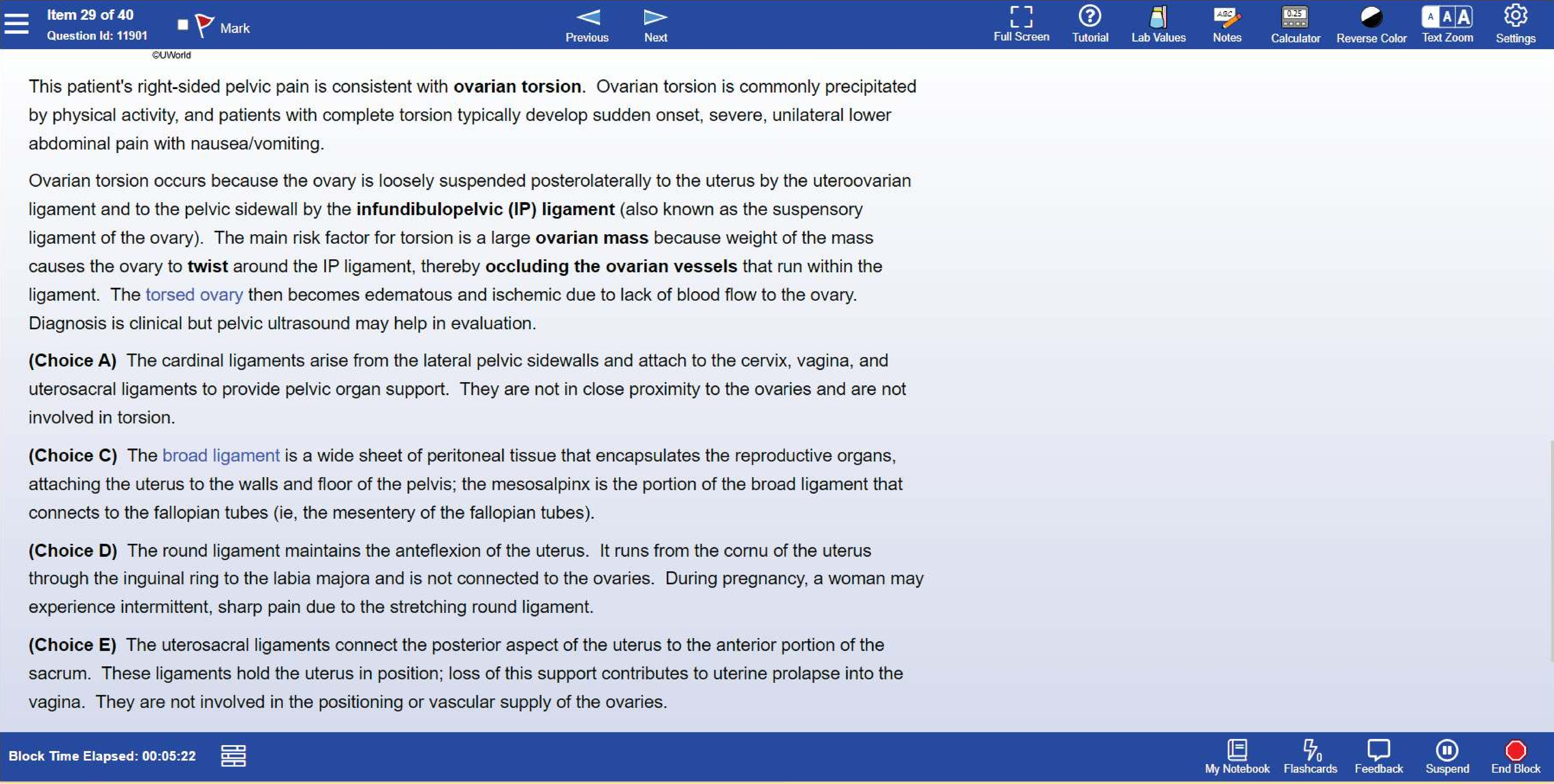

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This patient's right-sided pelvic pain is consistent with **ovarian torsion**. Ovarian torsion is commonly precipitated by physical activity, and patients with complete torsion typically develop sudden onset, severe, unilateral lower abdominal pain with nausea/vomiting.

Ovarian torsion occurs because the ovary is loosely suspended posterolaterally to the uterus by the uteroovarian ligament and to the pelvic sidewall by the **infundibulopelvic (IP) ligament** (also known as the suspensory ligament of the ovary). The main risk factor for torsion is a large **ovarian mass** because weight of the mass causes the ovary to **twist** around the IP ligament, thereby **occluding the ovarian vessels** that run within the ligament. The torsed ovary then becomes edematous and ischemic due to lack of blood flow to the ovary. Diagnosis is clinical but pelvic ultrasound may help in evaluation.

(Choice A) The cardinal ligaments arise from the lateral pelvic sidewalls and attach to the cervix, vagina, and uterosacral ligaments to provide pelvic organ support. They are not in close proximity to the ovaries and are not involved in torsion.

(Choice C) The broad ligament is a wide sheet of peritoneal tissue that encapsulates the reproductive organs, attaching the uterus to the walls and floor of the pelvis; the mesosalpinx is the portion of the broad ligament that connects to the fallopian tubes (ie, the mesentery of the fallopian tubes).

(Choice D) The round ligament maintains the anteflexion of the uterus. It runs from the cornu of the uterus through the inguinal ring to the labia majora and is not connected to the ovaries. During pregnancy, a woman may experience intermittent, sharp pain due to the stretching round ligament.

(Choice E) The uterosacral ligaments connect the posterior aspect of the uterus to the anterior portion of the sacrum. These ligaments hold the uterus in position; loss of this support contributes to uterine prolapse into the vagina. They are not involved in the positioning or vascular supply of the ovaries.

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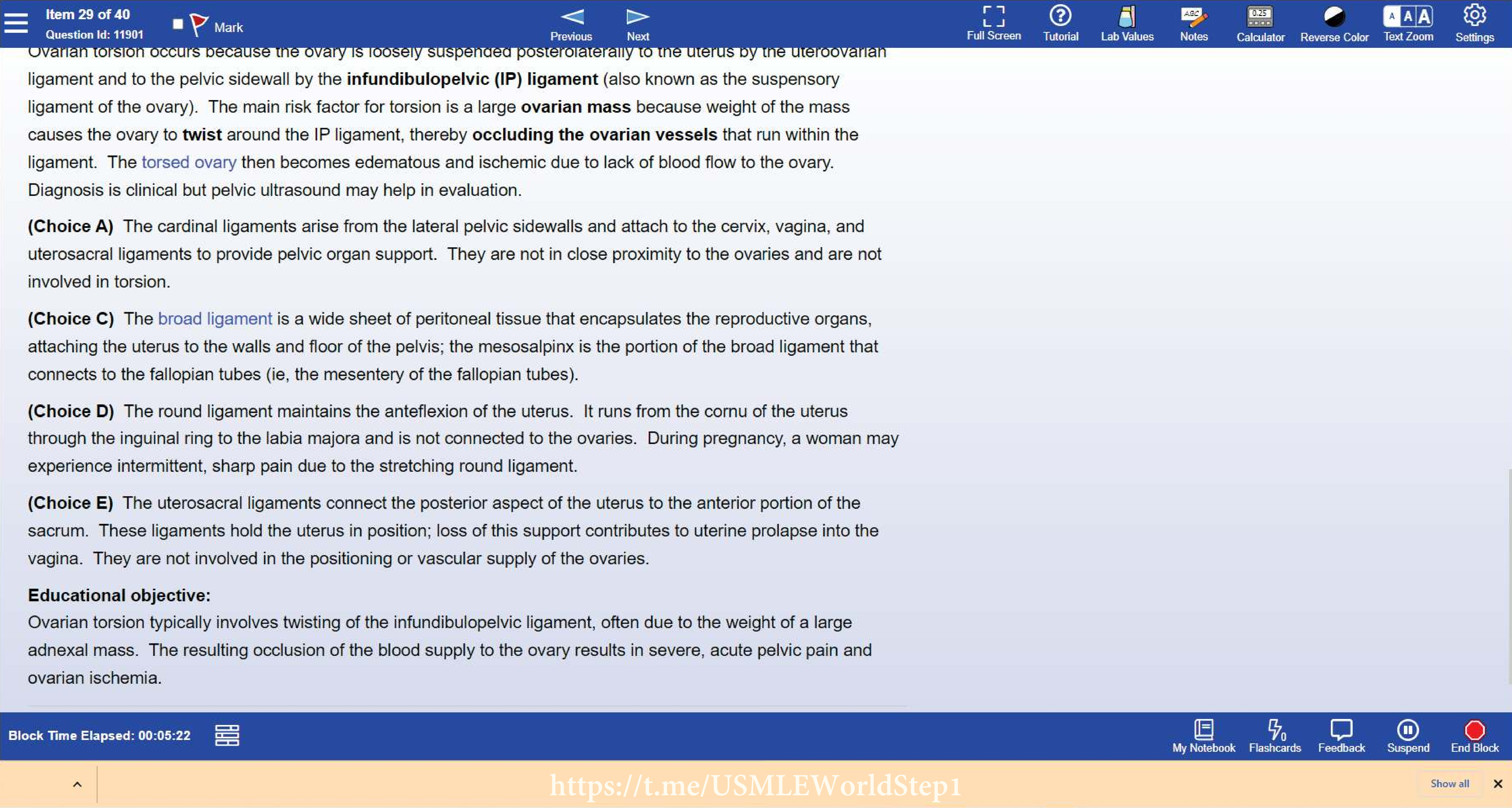


Ovarian torsion occurs because the ovary is loosely suspended posterolaterally to the uterus by the uteroovarian ligament and to the pelvic sidewall by the **infundibulopelvic (IP) ligament** (also known as the suspensory ligament of the ovary). The main risk factor for torsion is a large **ovarian mass** because weight of the mass causes the ovary to **twist** around the IP ligament, thereby **occluding the ovarian vessels** that run within the ligament. The torsed ovary then becomes edematous and ischemic due to lack of blood flow to the ovary. Diagnosis is clinical but pelvic ultrasound may help in evaluation.

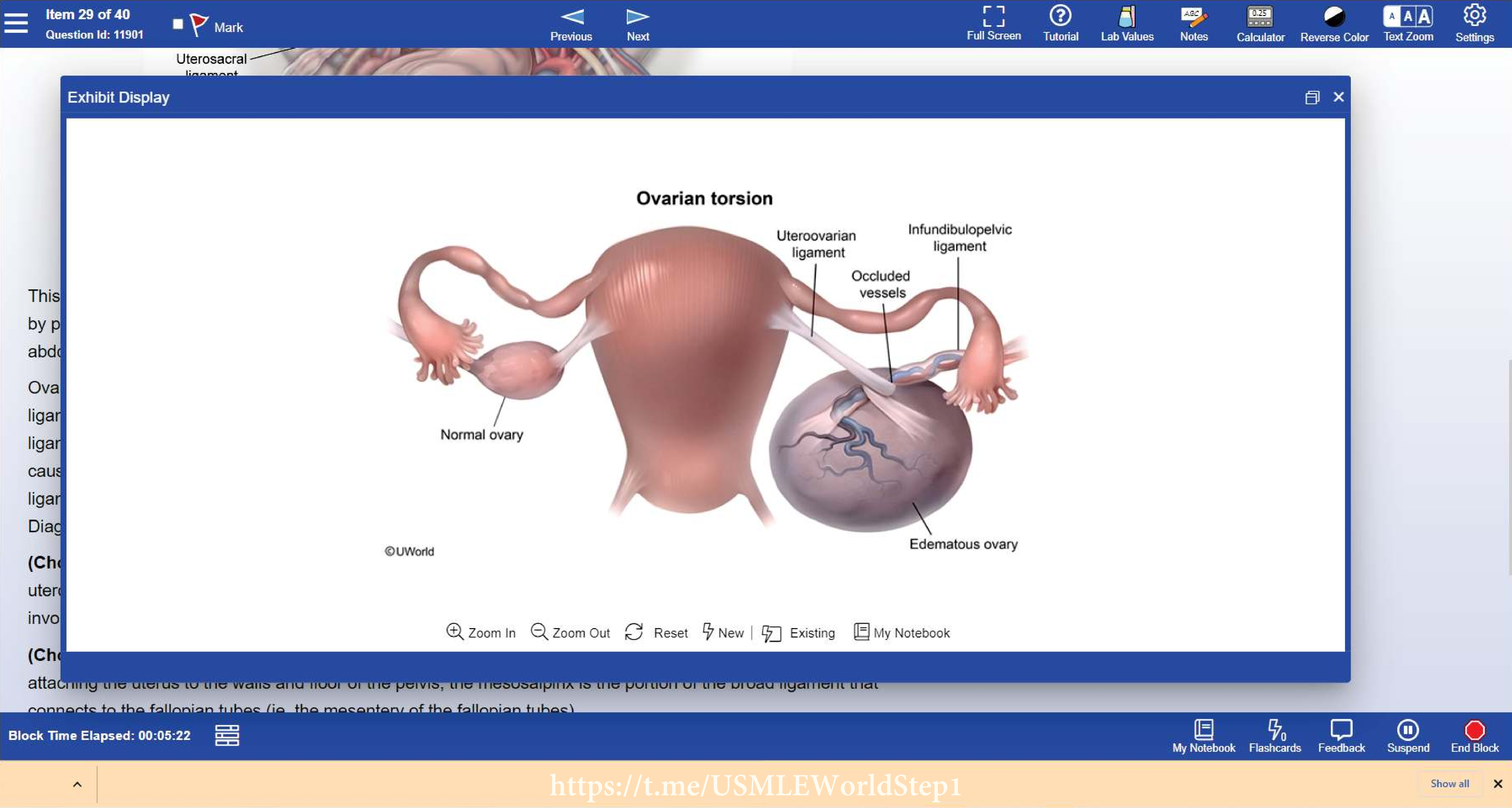
(Choice A) The cardinal ligaments arise from the lateral pelvic sidewalls and attach to the cervix, vagina, and uterosacral ligaments to provide pelvic organ support. They are not in close proximity to the ovaries and are not involved in torsion.

(Choice C) The broad ligament is a wide sheet of peritoneal tissue that encapsulates the reproductive organs, attaching the uterus to the walls and floor of the pelvis; the mesosalpinx is the portion of the broad ligament that connects to the fallopian tubes (ie, the mesentery of the fallopian tubes).

(Choice D) The round ligament maintains the anteflexion of the uterus. It runs from the cornu of the uterus through the inguinal ring to the labia majora and is not connected to the ovaries. During pregnancy, a woman may experience intermittent, sharp pain due to the stretching round ligament.

(Choice E) The uterosacral ligaments connect the posterior aspect of the uterus to the anterior portion of the sacrum. These ligaments hold the uterus in position; loss of this support contributes to uterine prolapse into the vagina. They are not involved in the positioning or vascular supply of the ovaries.

Educational objective:
Ovarian torsion typically involves twisting of the infundibulopelvic ligament, often due to the weight of a large adnexal mass. The resulting occlusion of the blood supply to the ovary results in severe, acute pelvic pain and ovarian ischemia.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Uterosacral
ligament
Exhibit Display
Ovarian torsion
Uteroovarian ligament
Infundibulopelvic ligament
Occluded vessels
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attaching the uterus to the walls and floor of the pelvis, the mesosalpinx is the portion of the broad ligament that connects to the fallopian tubes (ie, the mesentery of the fallopian tubes).

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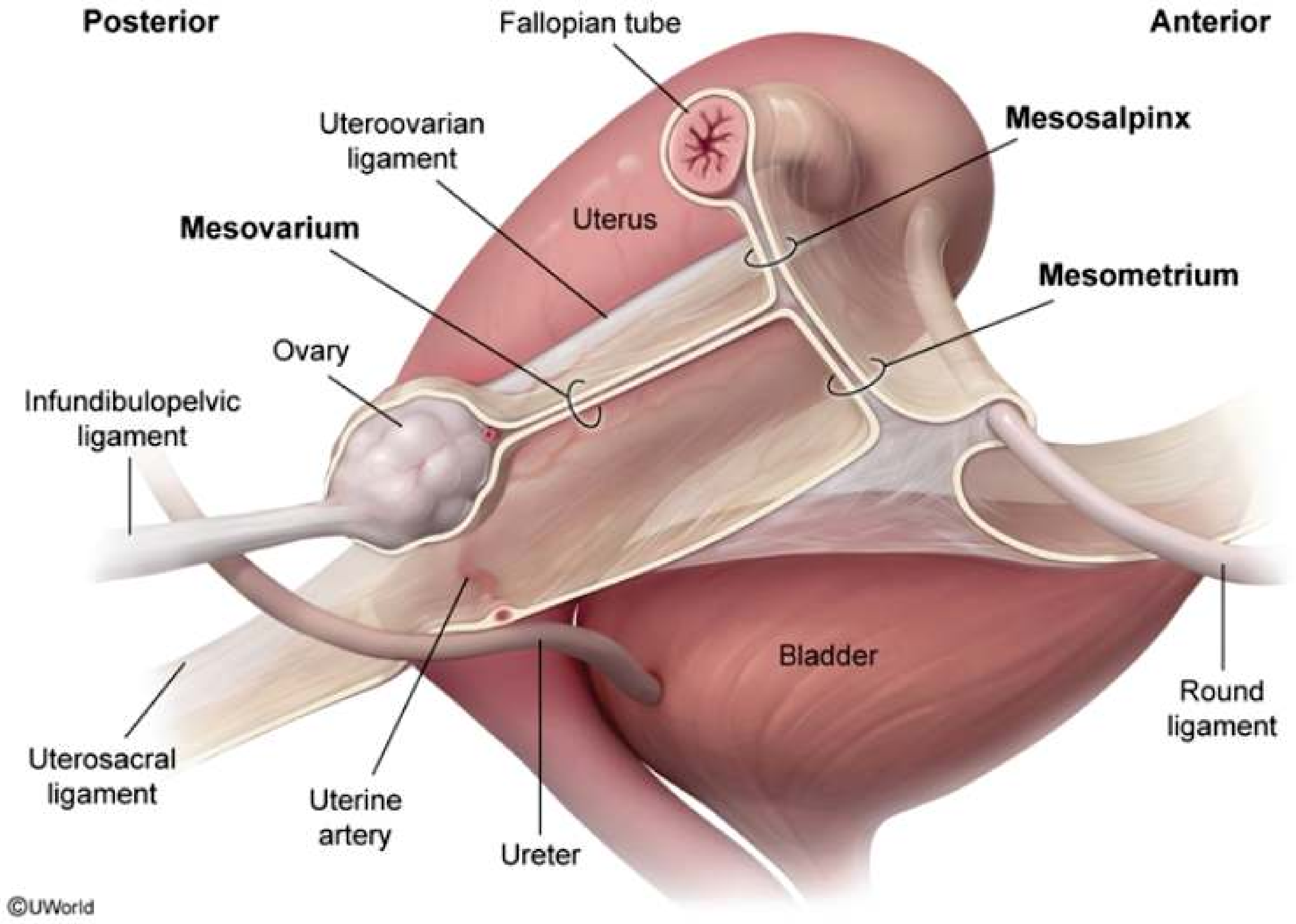
Anatomy of the broad ligament


Posterior
Fallopian tube
Anterior
Uteroovarian ligament
Mesosalpinx
Mesovarium
Uterus
Mesometrium
Ovary
Infundibulopelvic ligament
Bladder
Round ligament
Uterosacral ligament
Uterine artery
Ureter
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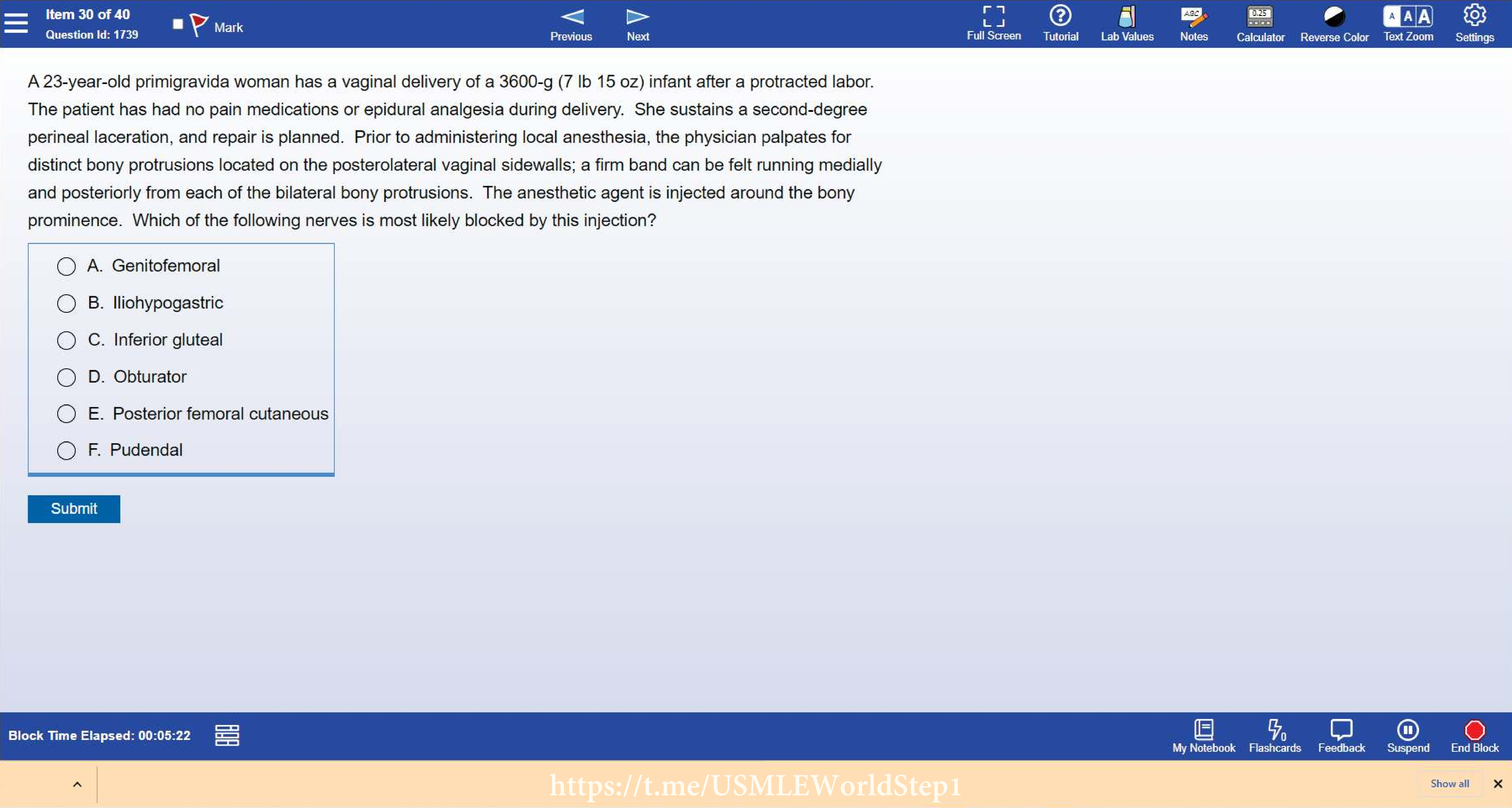
sacrum. These ligaments hold the uterus in position; loss of this support contributes to uterine prolapse into the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A 23-year-old primigravida woman has a vaginal delivery of a 3600-g (7 lb 15 oz) infant after a protracted labor. The patient has had no pain medications or epidural analgesia during delivery. She sustains a second-degree perineal laceration, and repair is planned. Prior to administering local anesthesia, the physician palpates for distinct bony protrusions located on the posterolateral vaginal sidewalls; a firm band can be felt running medially and posteriorly from each of the bilateral bony protrusions. The anesthetic agent is injected around the bony prominence. Which of the following nerves is most likely blocked by this injection?

○ A. Genitofemoral
○ B. Iliohypogastric
○ C. Inferior gluteal
○ D. Obturator
○ E. Posterior femoral cutaneous
○ F. Pudendal

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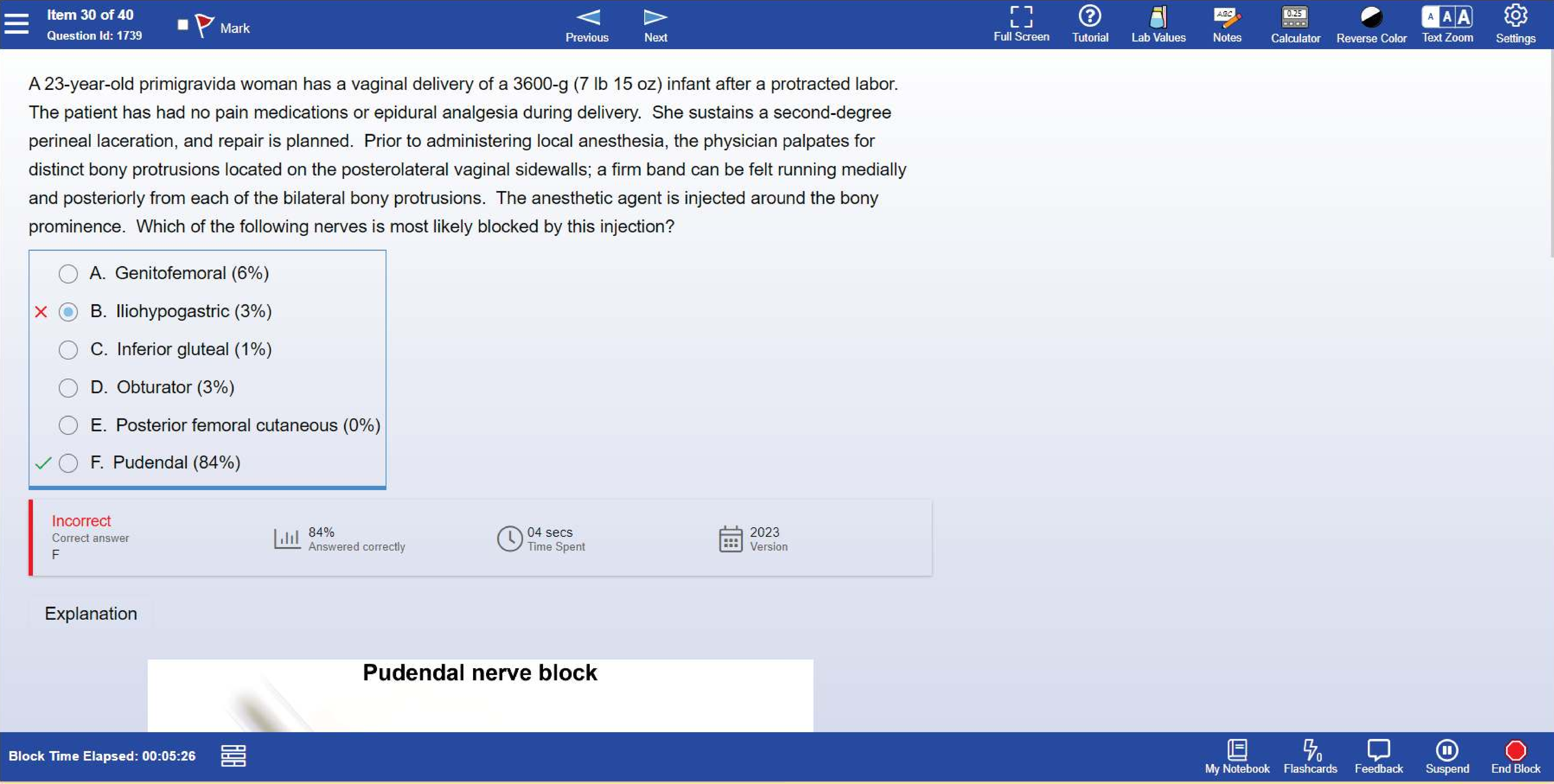
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- ○ A. Genitofemoral (6%)
- ✗ ● B. Iliohypogastric (3%)
- ○ C. Inferior gluteal (1%)
- ○ D. Obturator (3%)
- ○ E. Posterior femoral cutaneous (0%)
- ✓ ○ F. Pudendal (84%)

Incorrect
Correct answer
F

84%
Answered correctly

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Explanation

Pudendal nerve block

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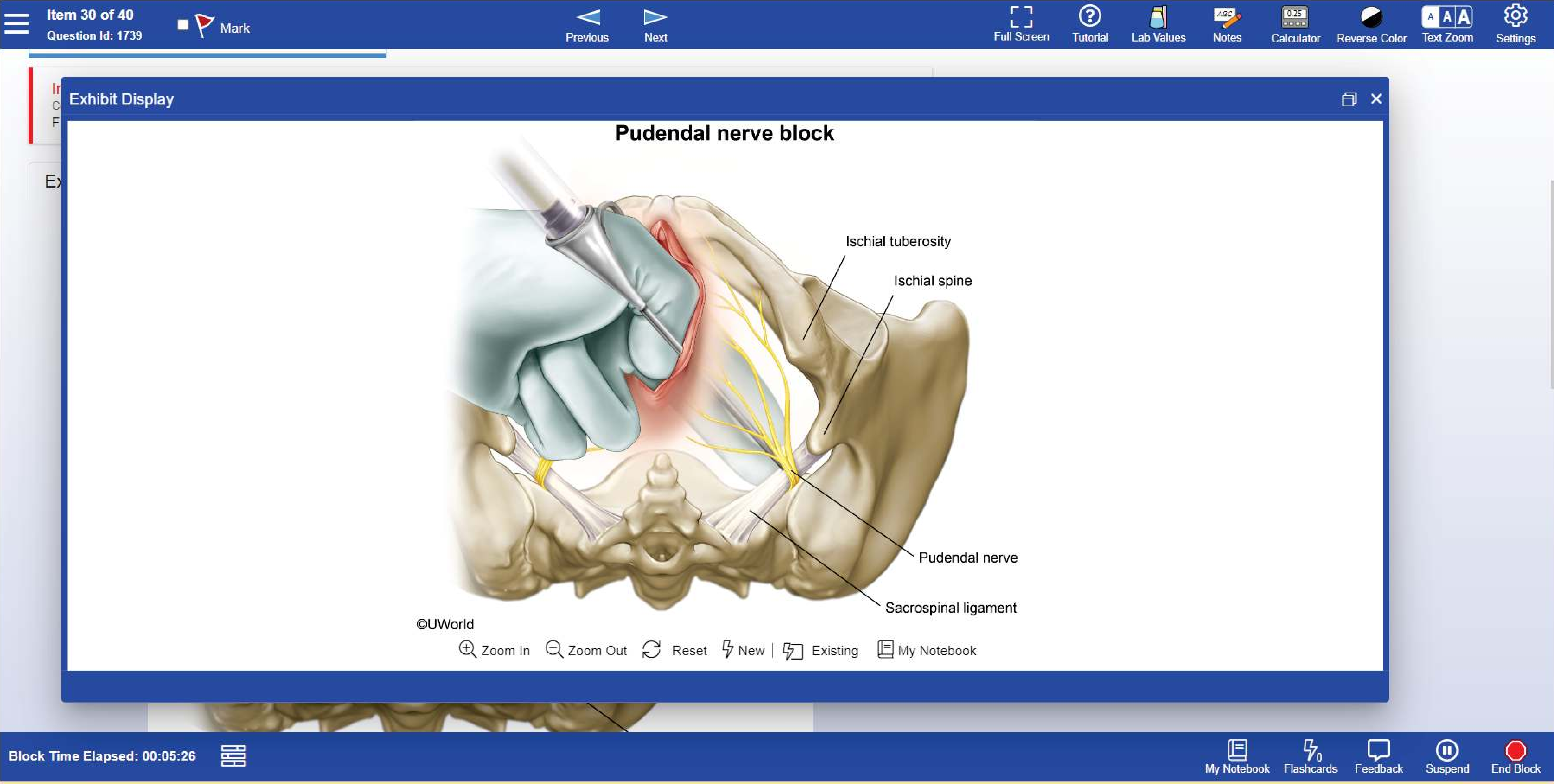

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Exhibit Display

Pudendal nerve block

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Ischial spine
Pudendal nerve
Sacrospinal ligament
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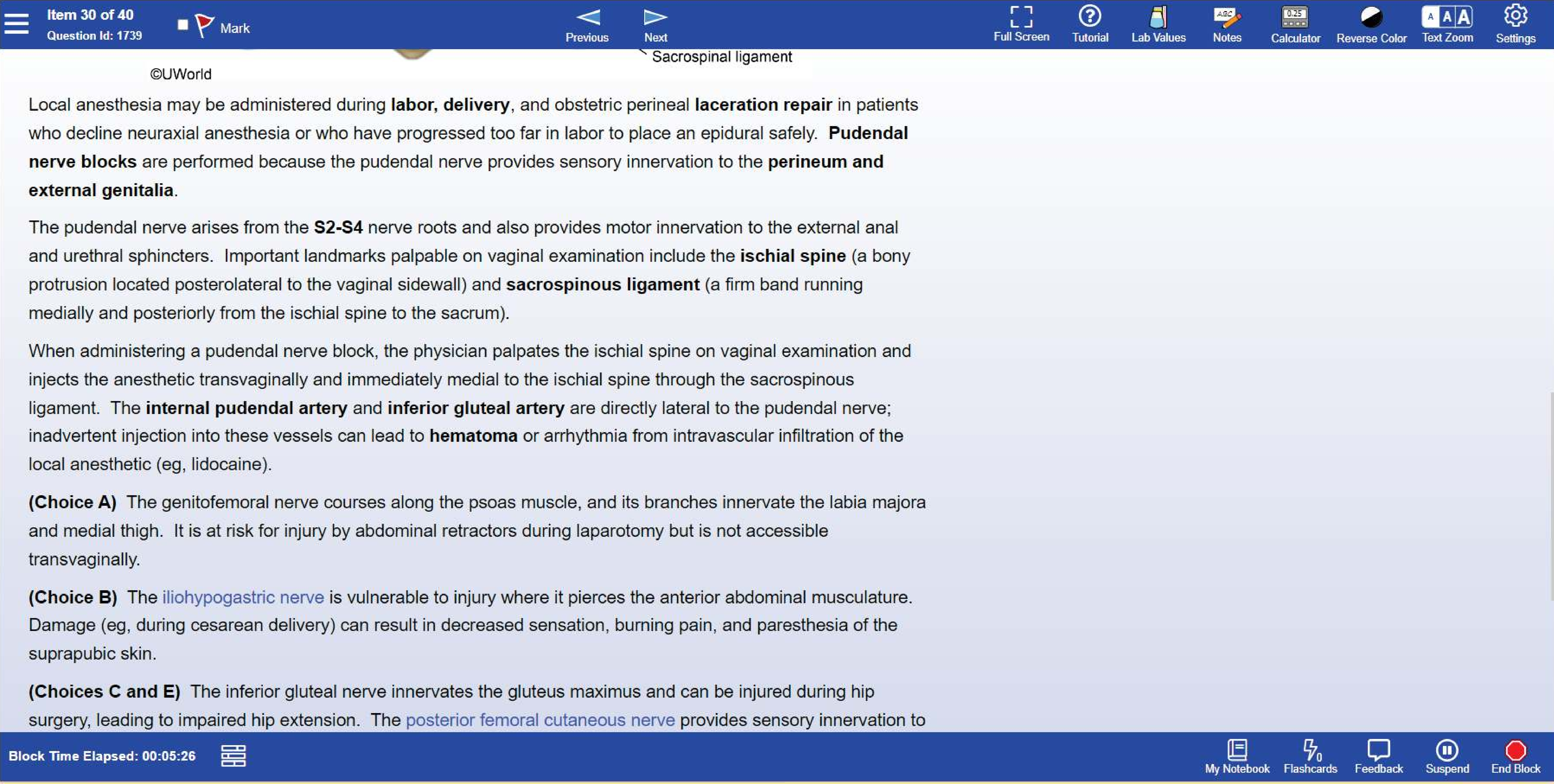
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Sacrospinal ligament
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Local anesthesia may be administered during **labor, delivery**, and obstetric perineal **laceration repair** in patients who decline neuraxial anesthesia or who have progressed too far in labor to place an epidural safely. **Pudendal nerve blocks** are performed because the pudendal nerve provides sensory innervation to the **perineum and external genitalia**.

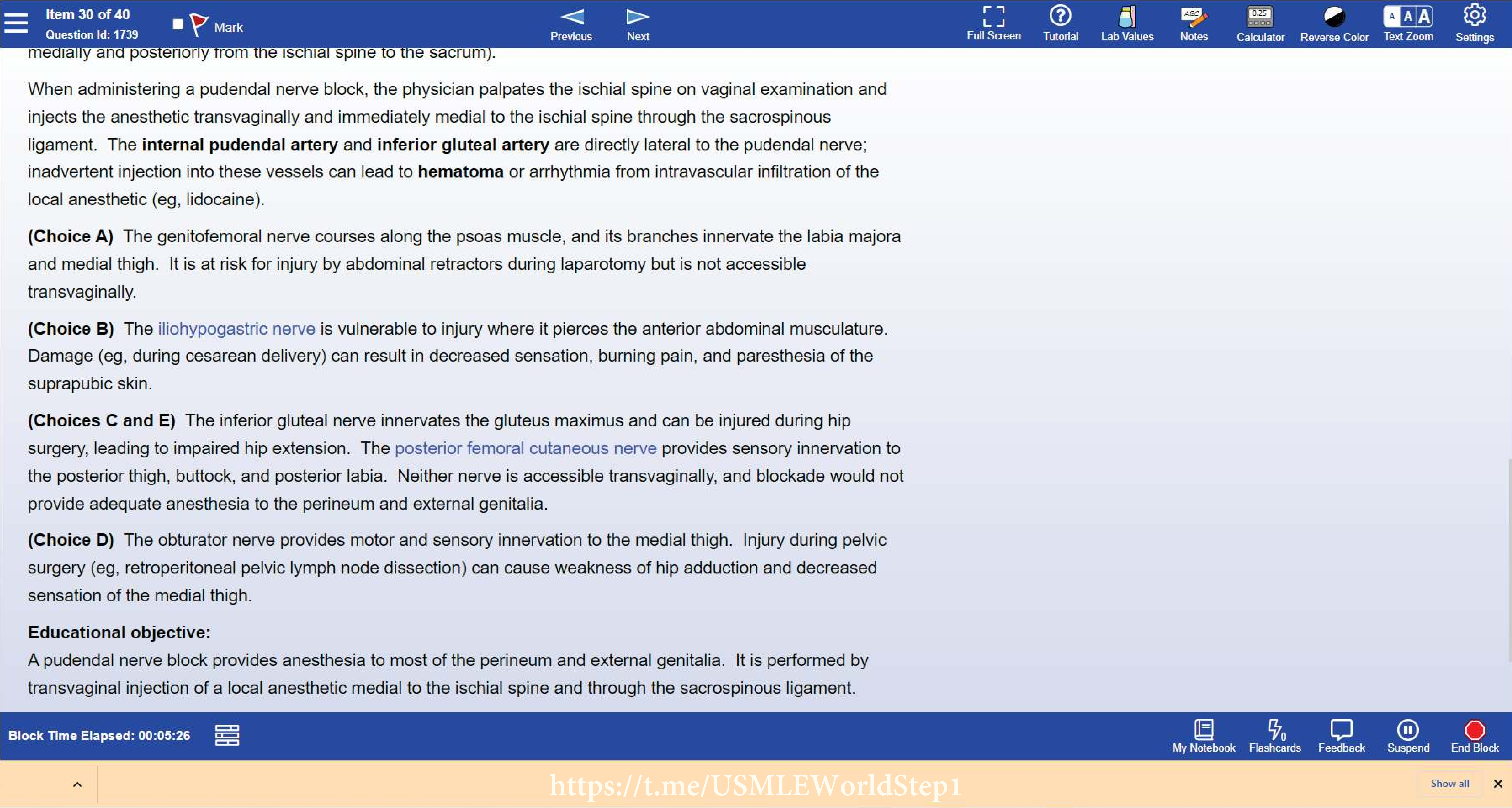
The pudendal nerve arises from the **S2-S4** nerve roots and also provides motor innervation to the external anal and urethral sphincters. Important landmarks palpable on vaginal examination include the **ischial spine** (a bony protrusion located posterolateral to the vaginal sidewall) and **sacrospinous ligament** (a firm band running medially and posteriorly from the ischial spine to the sacrum).

When administering a pudendal nerve block, the physician palpates the ischial spine on vaginal examination and injects the anesthetic transvaginally and immediately medial to the ischial spine through the sacrospinous ligament. The **internal pudendal artery** and **inferior gluteal artery** are directly lateral to the pudendal nerve; inadvertent injection into these vessels can lead to **hematoma** or arrhythmia from intravascular infiltration of the local anesthetic (eg, lidocaine).

(Choice A) The genitofemoral nerve courses along the psoas muscle, and its branches innervate the labia majora and medial thigh. It is at risk for injury by abdominal retractors during laparotomy but is not accessible transvaginally.

(Choice B) The iliohypogastric nerve is vulnerable to injury where it pierces the anterior abdominal musculature. Damage (eg, during cesarean delivery) can result in decreased sensation, burning pain, and paresthesia of the suprapubic skin.

(Choices C and E) The inferior gluteal nerve innervates the gluteus maximus and can be injured during hip surgery, leading to impaired hip extension. The posterior femoral cutaneous nerve provides sensory innervation to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medially and posteriorly from the ischial spine to the sacrum).

When administering a pudendal nerve block, the physician palpates the ischial spine on vaginal examination and injects the anesthetic transvaginally and immediately medial to the ischial spine through the sacrospinous ligament. The **internal pudendal artery** and **inferior gluteal artery** are directly lateral to the pudendal nerve; inadvertent injection into these vessels can lead to **hematoma** or arrhythmia from intravascular infiltration of the local anesthetic (eg, lidocaine).

(Choice A) The genitofemoral nerve courses along the psoas muscle, and its branches innervate the labia majora and medial thigh. It is at risk for injury by abdominal retractors during laparotomy but is not accessible transvaginally.

(Choice B) The iliohypogastric nerve is vulnerable to injury where it pierces the anterior abdominal musculature. Damage (eg, during cesarean delivery) can result in decreased sensation, burning pain, and paresthesia of the suprapubic skin.

(Choices C and E) The inferior gluteal nerve innervates the gluteus maximus and can be injured during hip surgery, leading to impaired hip extension. The posterior femoral cutaneous nerve provides sensory innervation to the posterior thigh, buttock, and posterior labia. Neither nerve is accessible transvaginally, and blockade would not provide adequate anesthesia to the perineum and external genitalia.

(Choice D) The obturator nerve provides motor and sensory innervation to the medial thigh. Injury during pelvic surgery (eg, retroperitoneal pelvic lymph node dissection) can cause weakness of hip adduction and decreased sensation of the medial thigh.

Educational objective:
A pudendal nerve block provides anesthesia to most of the perineum and external genitalia. It is performed by transvaginal injection of a local anesthetic medial to the ischial spine and through the sacrospinous ligament.

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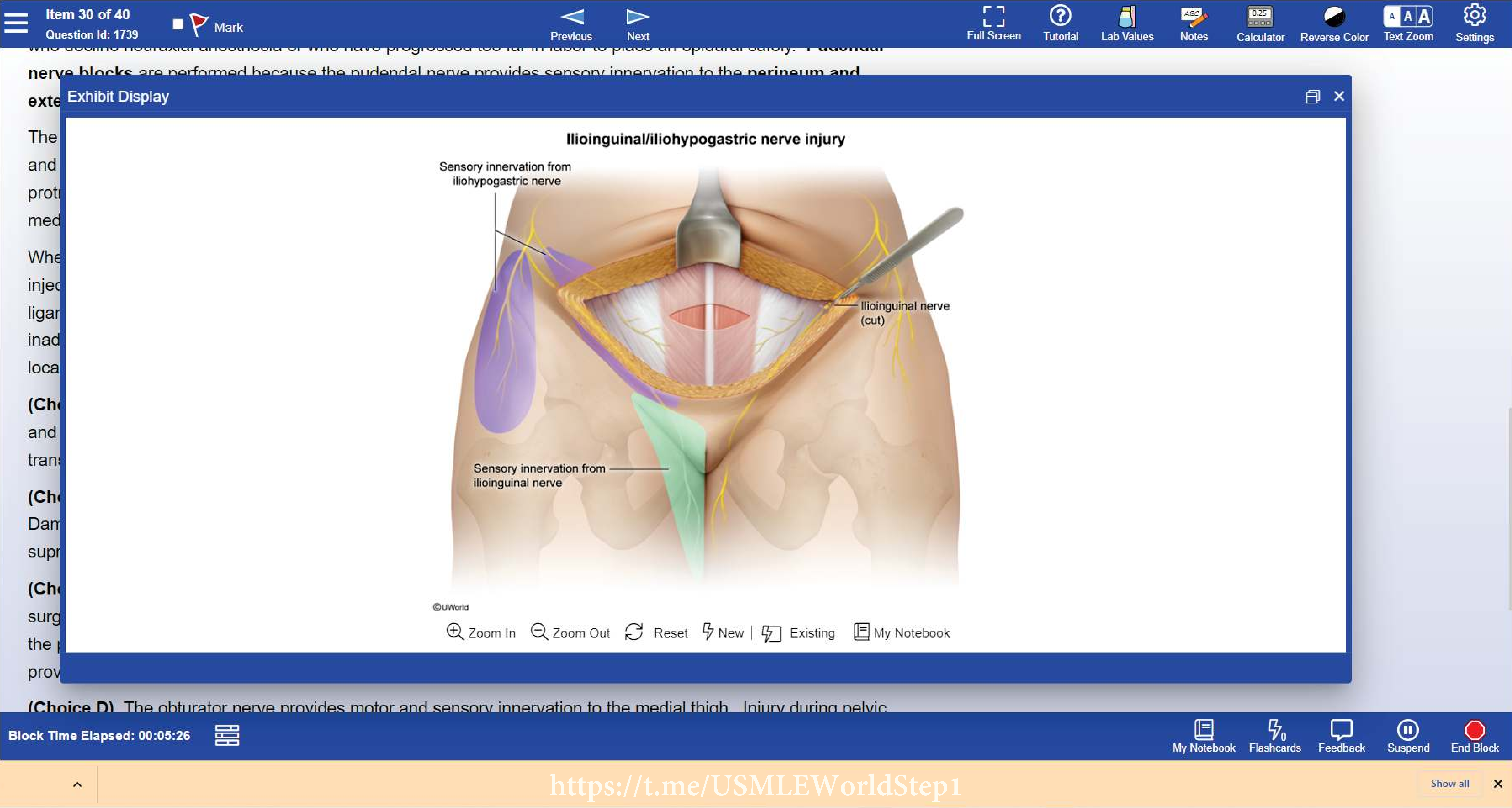
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Exhibit Display
Ilioinguinal/iliohypogastric nerve injury
Sensory innervation from iliohypogastric nerve
Ilioinguinal nerve (cut)
Sensory innervation from ilioinguinal nerve
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who decline neuraxial anesthesia or who have progressed too far in labor to place an epidural safely. **Pudendal nerve blocks** are performed because the pudendal nerve provides sensory innervation to the **perineum and exte**

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(Choice D) The obturator nerve provides motor and sensory innervation to the medial thigh. Injury during pelvic

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medially and posteriorly from the ischial spine to the sacrum).

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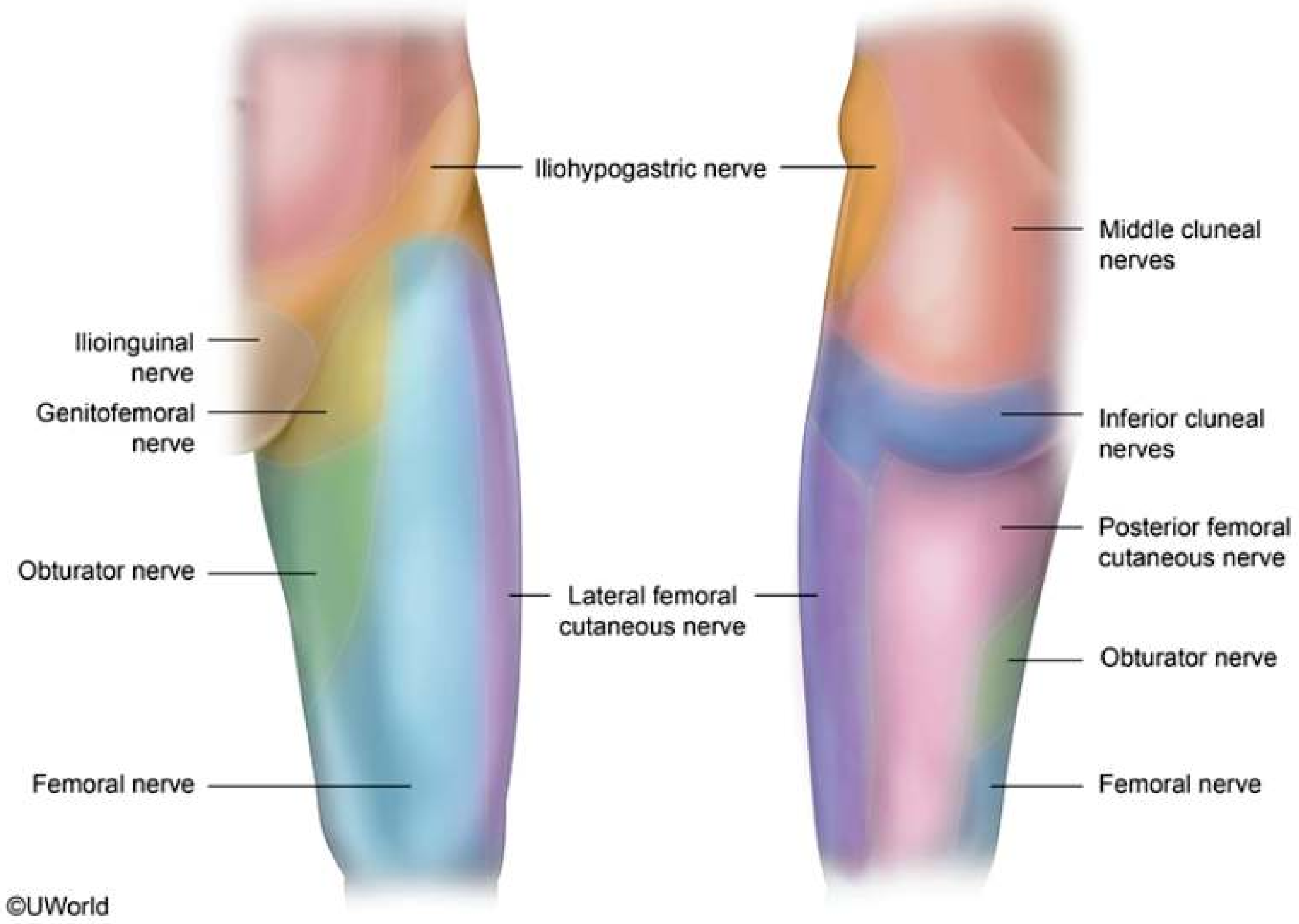
Abdominopelvic cutaneous innervation


Iliohypogastric nerve
Middle cluneal nerves
Ilioinguinal nerve
Genitofemoral nerve
Inferior cluneal nerves
Posterior femoral cutaneous nerve
Obturator nerve
Lateral femoral cutaneous nerve
Obturator nerve
Femoral nerve
Femoral nerve

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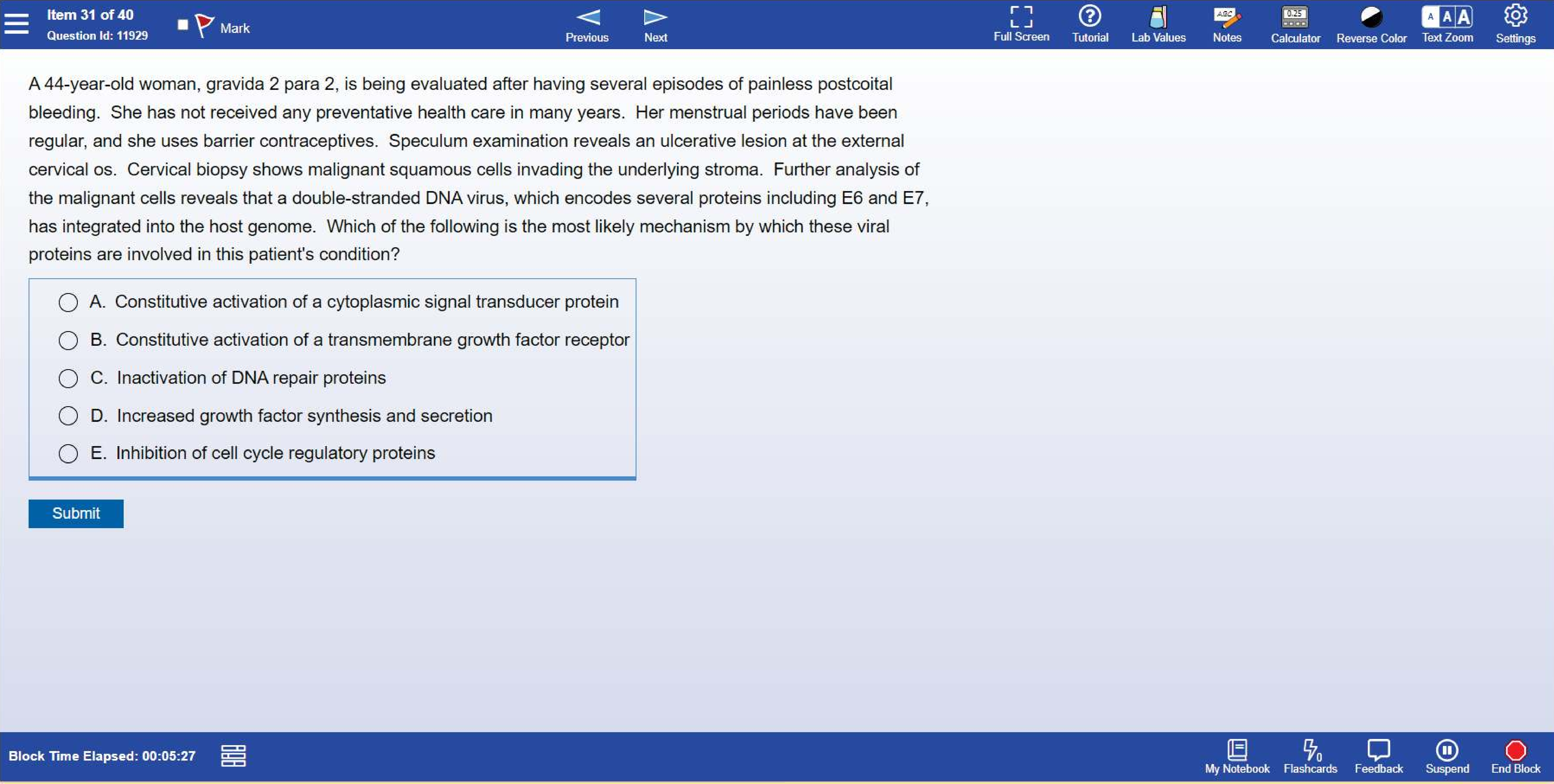
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A 44-year-old woman, gravida 2 para 2, is being evaluated after having several episodes of painless postcoital bleeding. She has not received any preventative health care in many years. Her menstrual periods have been regular, and she uses barrier contraceptives. Speculum examination reveals an ulcerative lesion at the external cervical os. Cervical biopsy shows malignant squamous cells invading the underlying stroma. Further analysis of the malignant cells reveals that a double-stranded DNA virus, which encodes several proteins including E6 and E7, has integrated into the host genome. Which of the following is the most likely mechanism by which these viral proteins are involved in this patient's condition?

○ A. Constitutive activation of a cytoplasmic signal transducer protein

○ B. Constitutive activation of a transmembrane growth factor receptor

○ C. Inactivation of DNA repair proteins

○ D. Increased growth factor synthesis and secretion

○ E. Inhibition of cell cycle regulatory proteins

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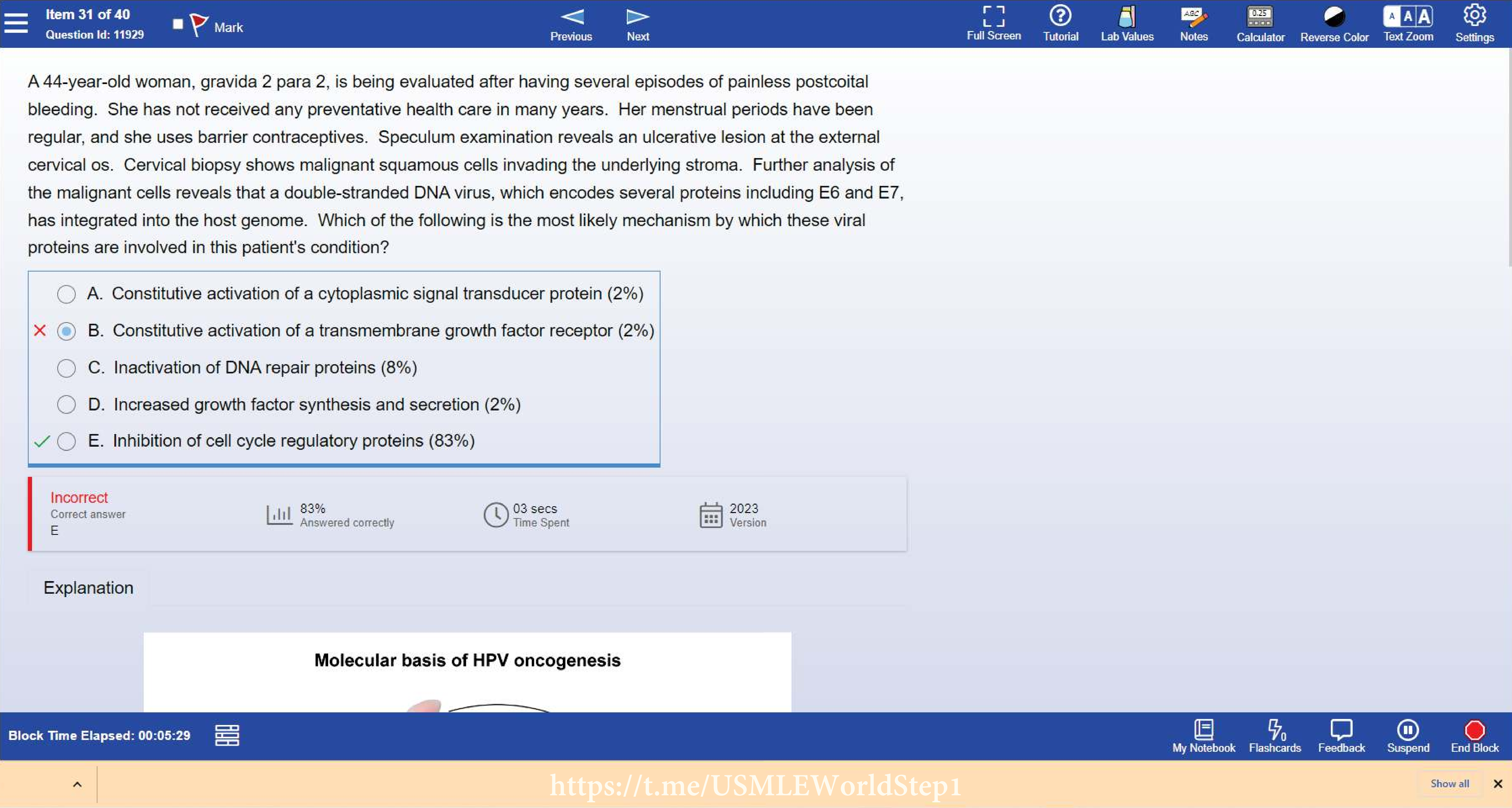
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○ A. Constitutive activation of a cytoplasmic signal transducer protein (2%)

✗ ● B. Constitutive activation of a transmembrane growth factor receptor (2%)

○ C. Inactivation of DNA repair proteins (8%)

○ D. Increased growth factor synthesis and secretion (2%)

✓ ○ E. Inhibition of cell cycle regulatory proteins (83%)

Incorrect
Correct answer
E

83%
Answered correctly

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Explanation

Molecular basis of HPV oncogenesis

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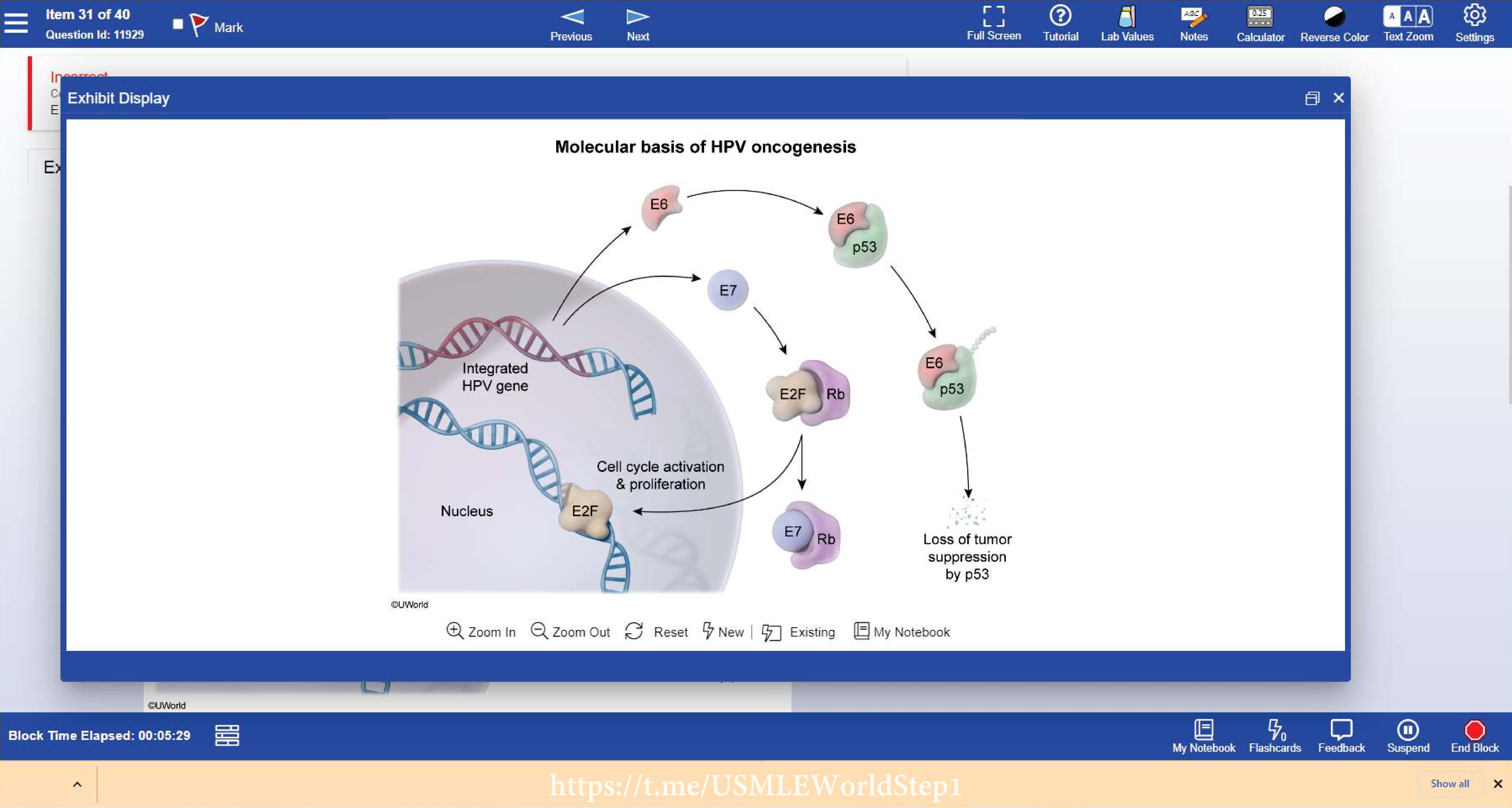

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Molecular basis of HPV oncogenesis

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E6
E6
p53
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Integrated
HPV gene
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Cell cycle activation
& proliferation
Nucleus
E2F
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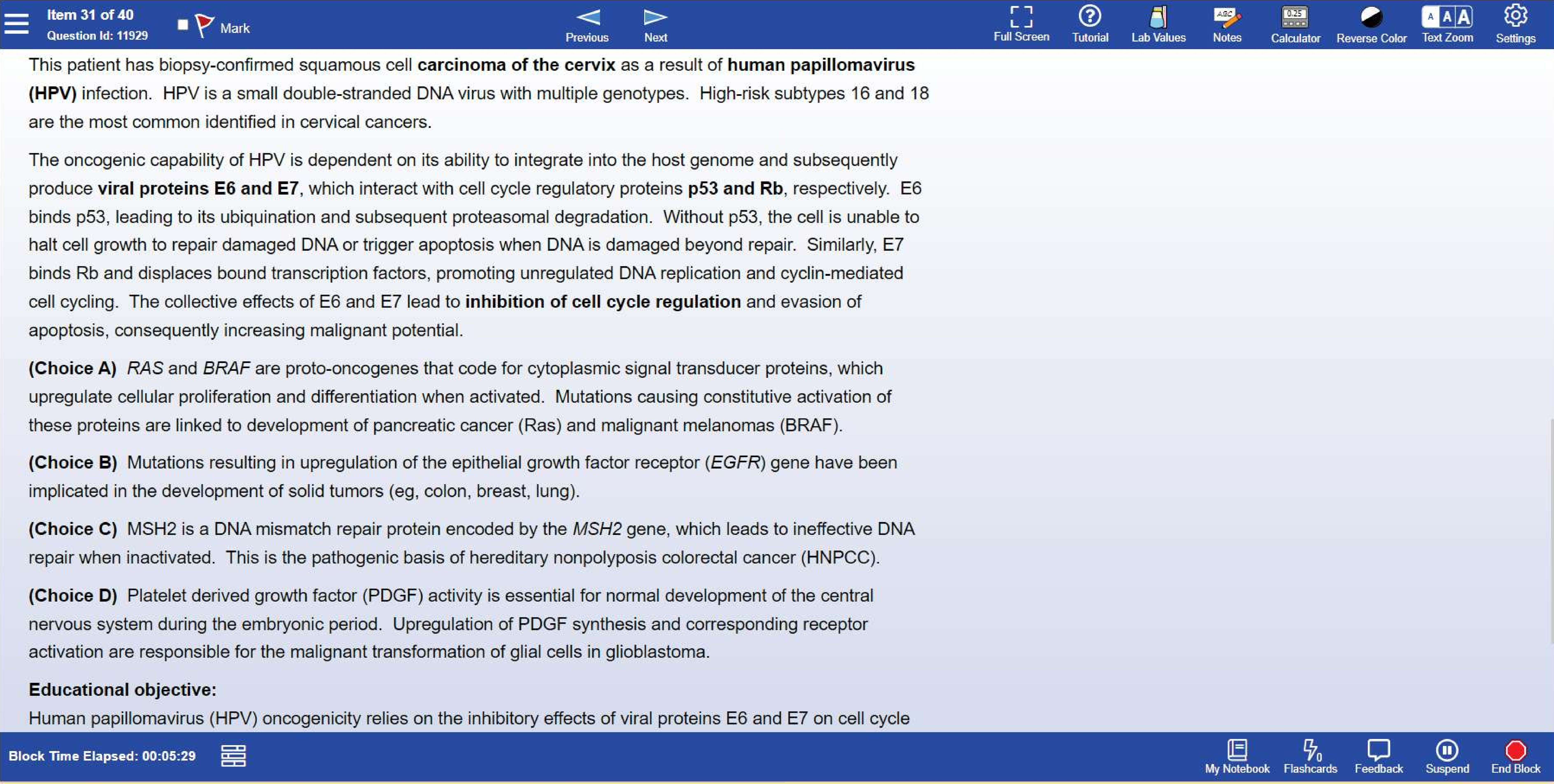


This patient has biopsy-confirmed squamous cell **carcinoma of the cervix** as a result of **human papillomavirus (HPV)** infection. HPV is a small double-stranded DNA virus with multiple genotypes. High-risk subtypes 16 and 18 are the most common identified in cervical cancers.

The oncogenic capability of HPV is dependent on its ability to integrate into the host genome and subsequently produce **viral proteins E6 and E7**, which interact with cell cycle regulatory proteins **p53 and Rb**, respectively. E6 binds p53, leading to its ubiquination and subsequent proteasomal degradation. Without p53, the cell is unable to halt cell growth to repair damaged DNA or trigger apoptosis when DNA is damaged beyond repair. Similarly, E7 binds Rb and displaces bound transcription factors, promoting unregulated DNA replication and cyclin-mediated cell cycling. The collective effects of E6 and E7 lead to **inhibition of cell cycle regulation** and evasion of apoptosis, consequently increasing malignant potential.

(Choice A) *RAS* and *BRAF* are proto-oncogenes that code for cytoplasmic signal transducer proteins, which upregulate cellular proliferation and differentiation when activated. Mutations causing constitutive activation of these proteins are linked to development of pancreatic cancer (Ras) and malignant melanomas (BRAF).

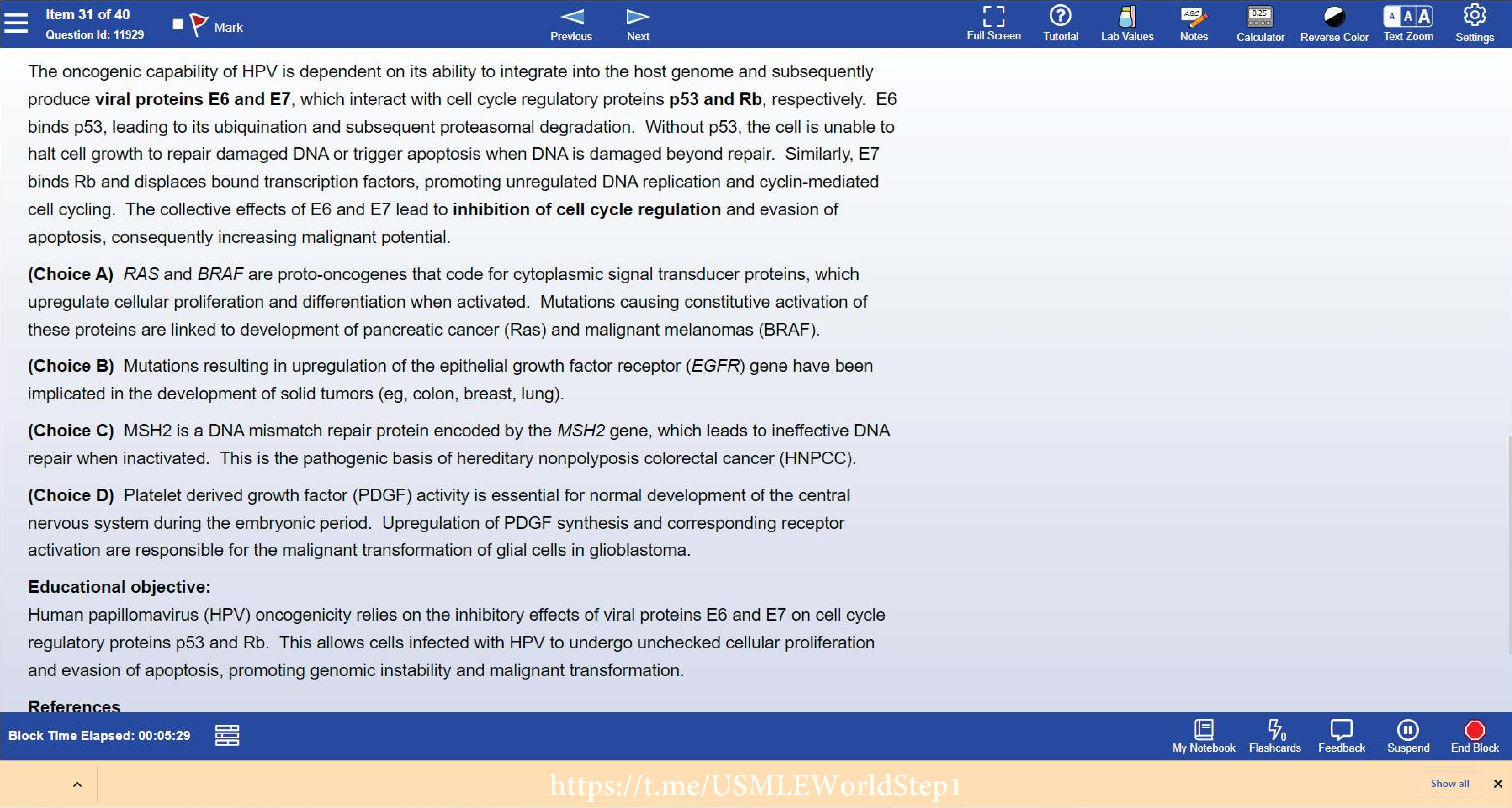
(Choice B) Mutations resulting in upregulation of the epithelial growth factor receptor (*EGFR*) gene have been implicated in the development of solid tumors (eg, colon, breast, lung).

(Choice C) MSH2 is a DNA mismatch repair protein encoded by the *MSH2* gene, which leads to ineffective DNA repair when inactivated. This is the pathogenic basis of hereditary nonpolyposis colorectal cancer (HNPCC).

(Choice D) Platelet derived growth factor (PDGF) activity is essential for normal development of the central nervous system during the embryonic period. Upregulation of PDGF synthesis and corresponding receptor activation are responsible for the malignant transformation of glial cells in glioblastoma.

Educational objective:

Human papillomavirus (HPV) oncogenicity relies on the inhibitory effects of viral proteins E6 and E7 on cell cycle



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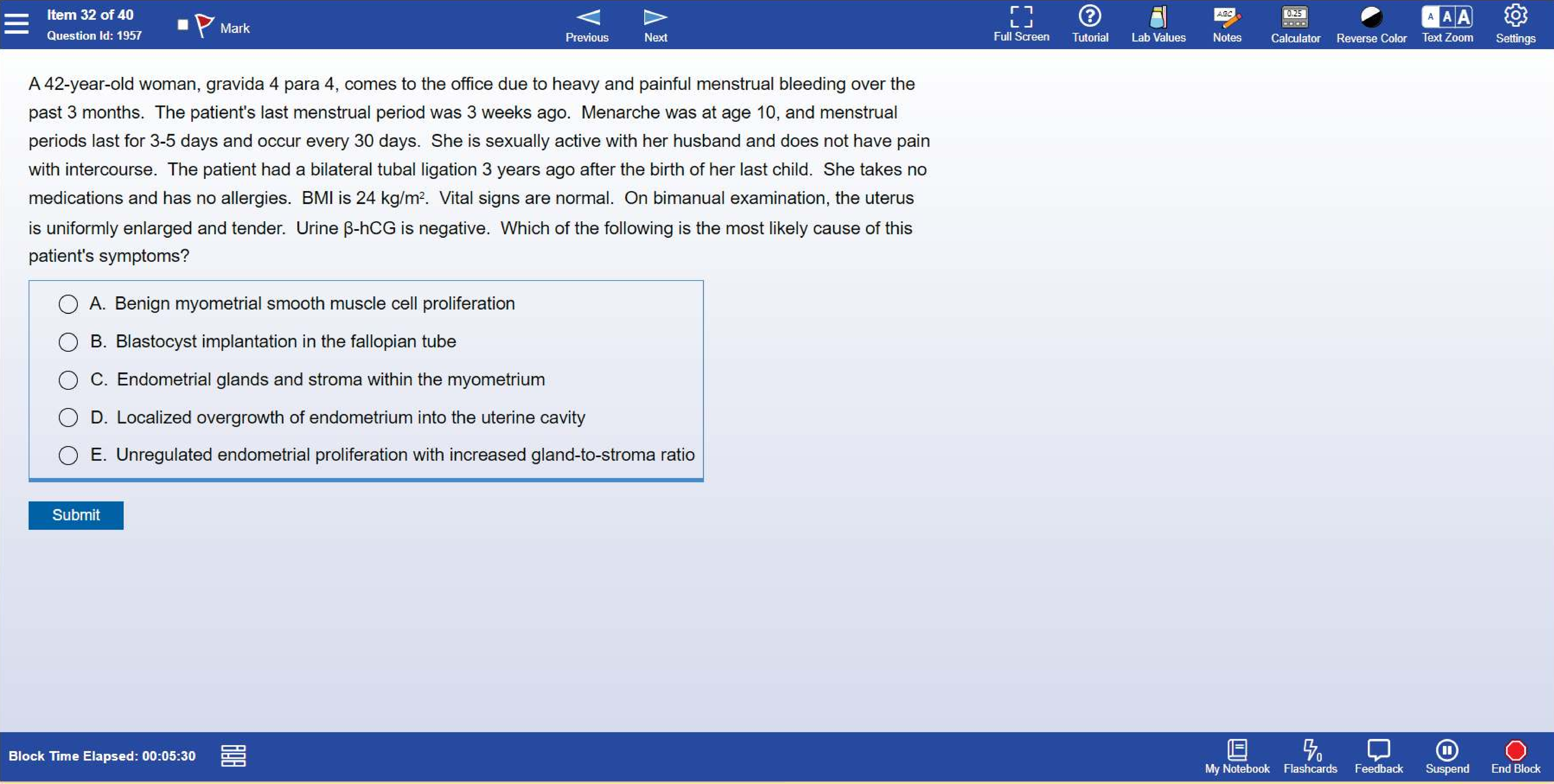
Educational objective:

Human papillomavirus (HPV) oncogenicity relies on the inhibitory effects of viral proteins E6 and E7 on cell cycle regulatory proteins p53 and Rb. This allows cells infected with HPV to undergo unchecked cellular proliferation and evasion of apoptosis, promoting genomic instability and malignant transformation.

References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A 42-year-old woman, gravida 4 para 4, comes to the office due to heavy and painful menstrual bleeding over the past 3 months. The patient's last menstrual period was 3 weeks ago. Menarche was at age 10, and menstrual periods last for 3-5 days and occur every 30 days. She is sexually active with her husband and does not have pain with intercourse. The patient had a bilateral tubal ligation 3 years ago after the birth of her last child. She takes no medications and has no allergies. BMI is 24 kg/m^2. Vital signs are normal. On bimanual examination, the uterus is uniformly enlarged and tender. Urine β-hCG is negative. Which of the following is the most likely cause of this patient's symptoms?

○ A. Benign myometrial smooth muscle cell proliferation

○ B. Blastocyst implantation in the fallopian tube

○ C. Endometrial glands and stroma within the myometrium

○ D. Localized overgrowth of endometrium into the uterine cavity

○ E. Unregulated endometrial proliferation with increased gland-to-stroma ratio

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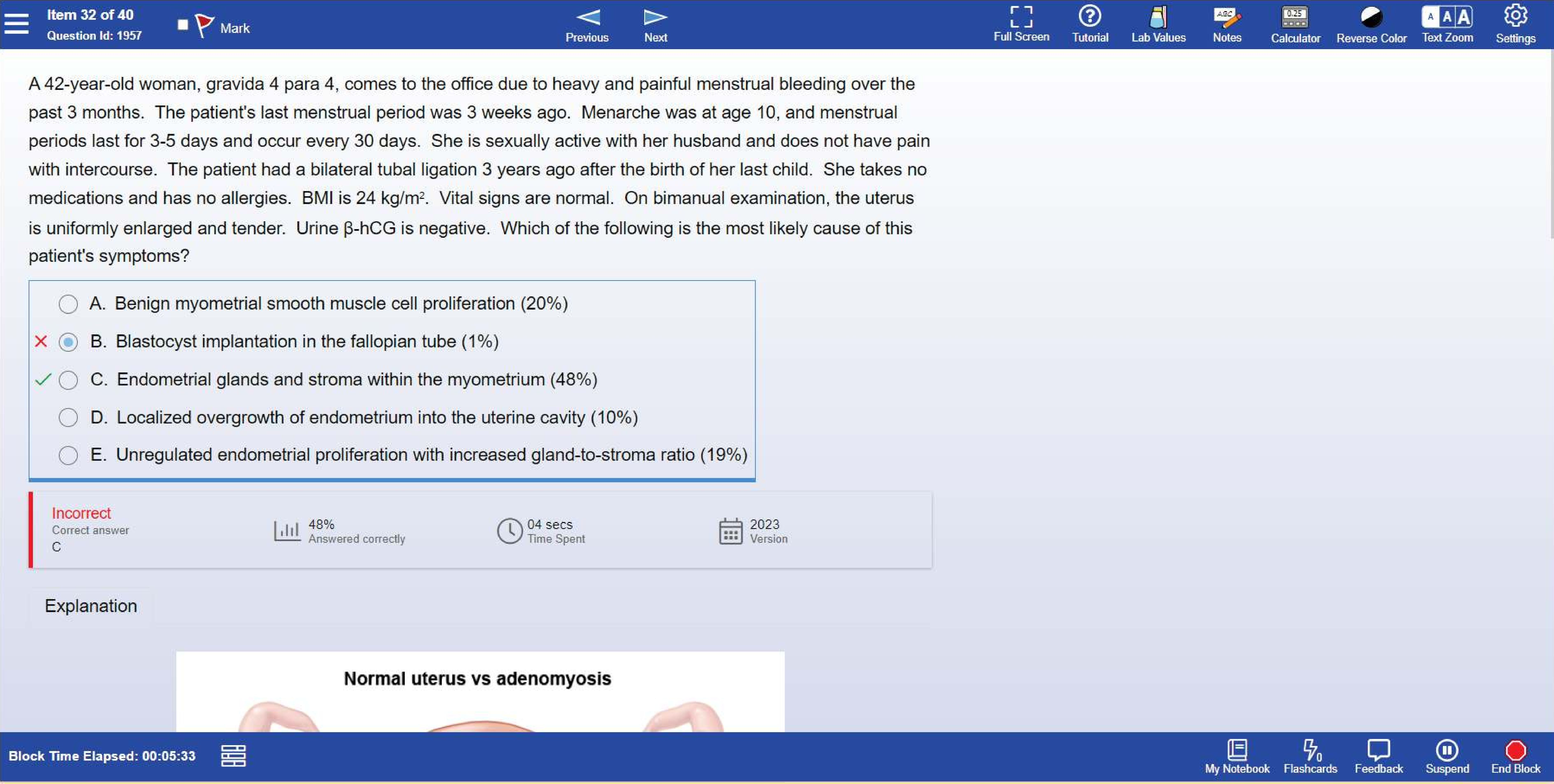
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- ○ A. Benign myometrial smooth muscle cell proliferation (20%)
- × ● B. Blastocyst implantation in the fallopian tube (1%)
- ✓ ○ C. Endometrial glands and stroma within the myometrium (48%)
- ○ D. Localized overgrowth of endometrium into the uterine cavity (10%)
- ○ E. Unregulated endometrial proliferation with increased gland-to-stroma ratio (19%)

Incorrect
Correct answer
C

48%
Answered correctly

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Explanation

Normal uterus vs adenomyosis

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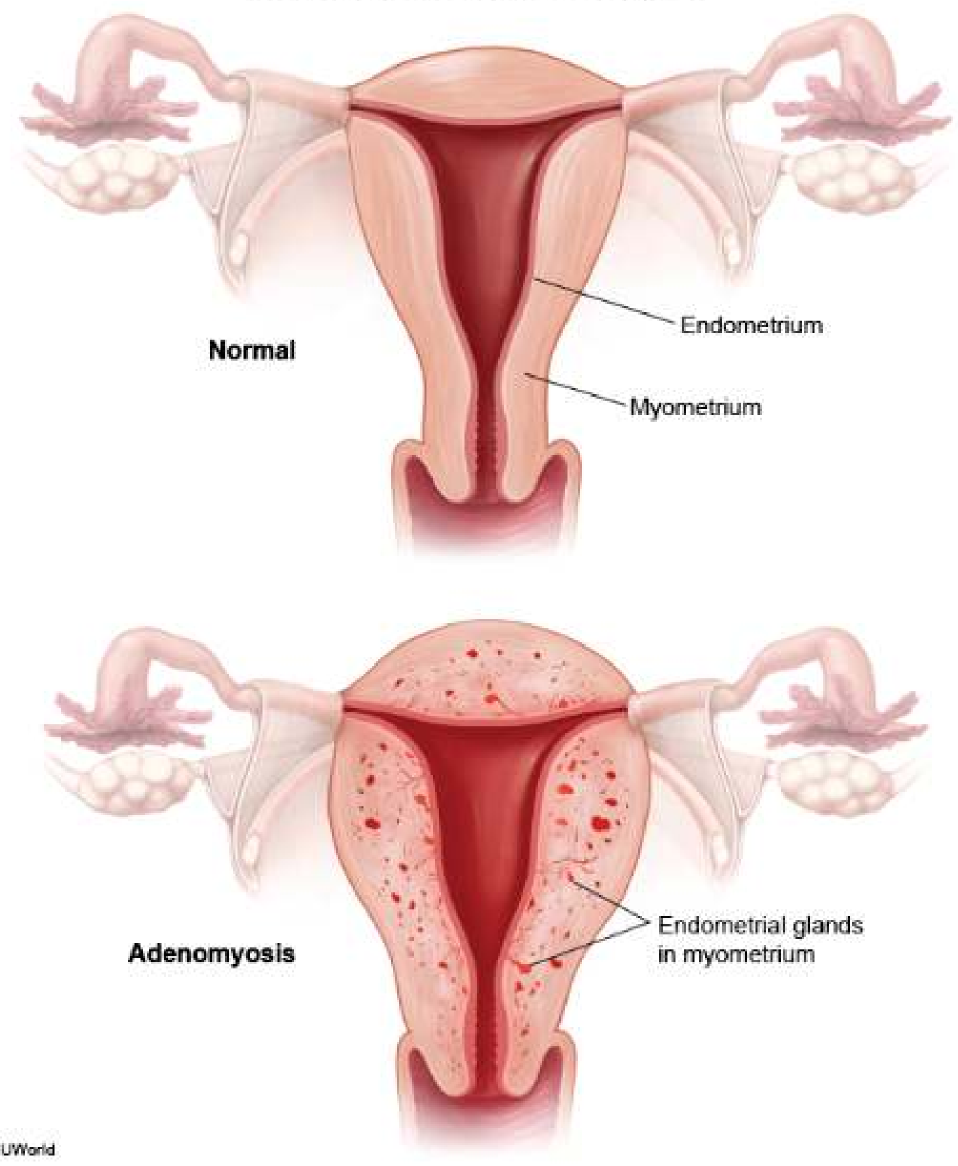
Normal uterus vs adenomyosis



Normal
Endometrium
Myometrium
Adenomyosis
Endometrial glands in myometrium
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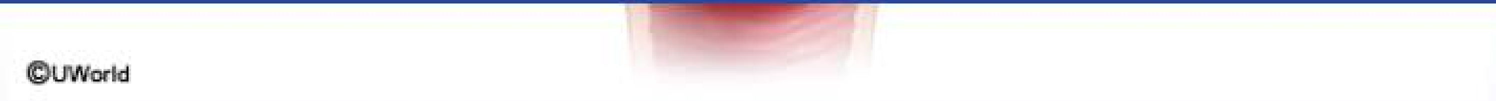

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This patient has **adenomyosis**, a disorder caused by an abnormal collection of **endometrial glands and stroma within the uterine myometrium**. Adenomyosis is common in multiparous women, and prior uterine surgery (eg, cesarean delivery) is a risk factor.

Although the exact pathogenesis is unclear, adenomyosis may occur due to endometrial invagination into the myometrium during periods of myometrial weakening or changes in vascularity at the endomyometrial interface (eg, pregnancy, uterine surgery). The clinical features of adenomyosis reflect its pathophysiology:

- endometrial gland proliferation and cyclic bleeding within the myometrium leads to **dysmenorrhea** and **uterine tenderness**
- abnormal myometrial hyperplasia and hypertrophy results in a concentric, **uniformly enlarged uterus**
- uterine enlargement and subsequently increased endometrial surface area causes **regular, heavy menstrual bleeding**

Definitive therapy is with hysterectomy, which allows for histologic diagnosis.

(Choice A) Leiomyomas (ie, uterine fibroids) are benign myometrial smooth muscle cell tumors. Although fibroids can cause regular, heavy menses (also due to increased endometrial surface area), the uterus is typically nontender and irregularly enlarged rather than tender and uniformly enlarged.

(Choice B) An ectopic pregnancy most commonly occurs due to abnormal blastocyst implantation in the fallopian tube. Although prior tubal surgery (eg, bilateral tubal ligation) is a risk factor, ectopic pregnancy is unlikely in this patient with a negative urine β-hCG. In addition, uterine enlargement would not be seen.

(Choice D) Endometrial polyps are benign, intracavitary, focal hyperplastic growths of endometrial tissue. In

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- uterine enlargement and subsequently increased endometrial surface area causes **regular, heavy menstrual bleeding**

Definitive therapy is with hysterectomy, which allows for histologic diagnosis.

(Choice A) Leiomyomas (ie, uterine fibroids) are benign myometrial smooth muscle cell tumors. Although fibroids can cause regular, heavy menses (also due to increased endometrial surface area), the uterus is typically nontender and irregularly enlarged rather than tender and uniformly enlarged.

(Choice B) An ectopic pregnancy most commonly occurs due to abnormal blastocyst implantation in the fallopian tube. Although prior tubal surgery (eg, bilateral tubal ligation) is a risk factor, ectopic pregnancy is unlikely in this patient with a negative urine β-hCG. In addition, uterine enlargement would not be seen.

(Choice D) Endometrial polyps are benign, intracavitary, focal hyperplastic growths of endometrial tissue. In contrast to adenomyosis, endometrial polyps cause painless intermenstrual bleeding rather than painful, cyclic, heavy menses. There is also no associated uterine tenderness or enlargement.

(Choice E) Patients with endometrial hyperplasia have unregulated endometrial gland proliferation with increased gland-to-stroma ratio; the thickened endometrial lining may slightly increase uterine size and cause heavy menses. However, endometrial hyperplasia does not typically cause dysmenorrhea or uterine tenderness. In addition, the most common risk factor is unopposed estrogen from chronic anovulation and/or obesity; this patient has regular menses and a normal BMI.

Educational objective:

Adenomyosis is the abnormal presence of endometrial glands and stroma within the uterine myometrium. Affected patients are typically multiparous women with dysmenorrhea, heavy menses, and a uniformly enlarged uterus.

References

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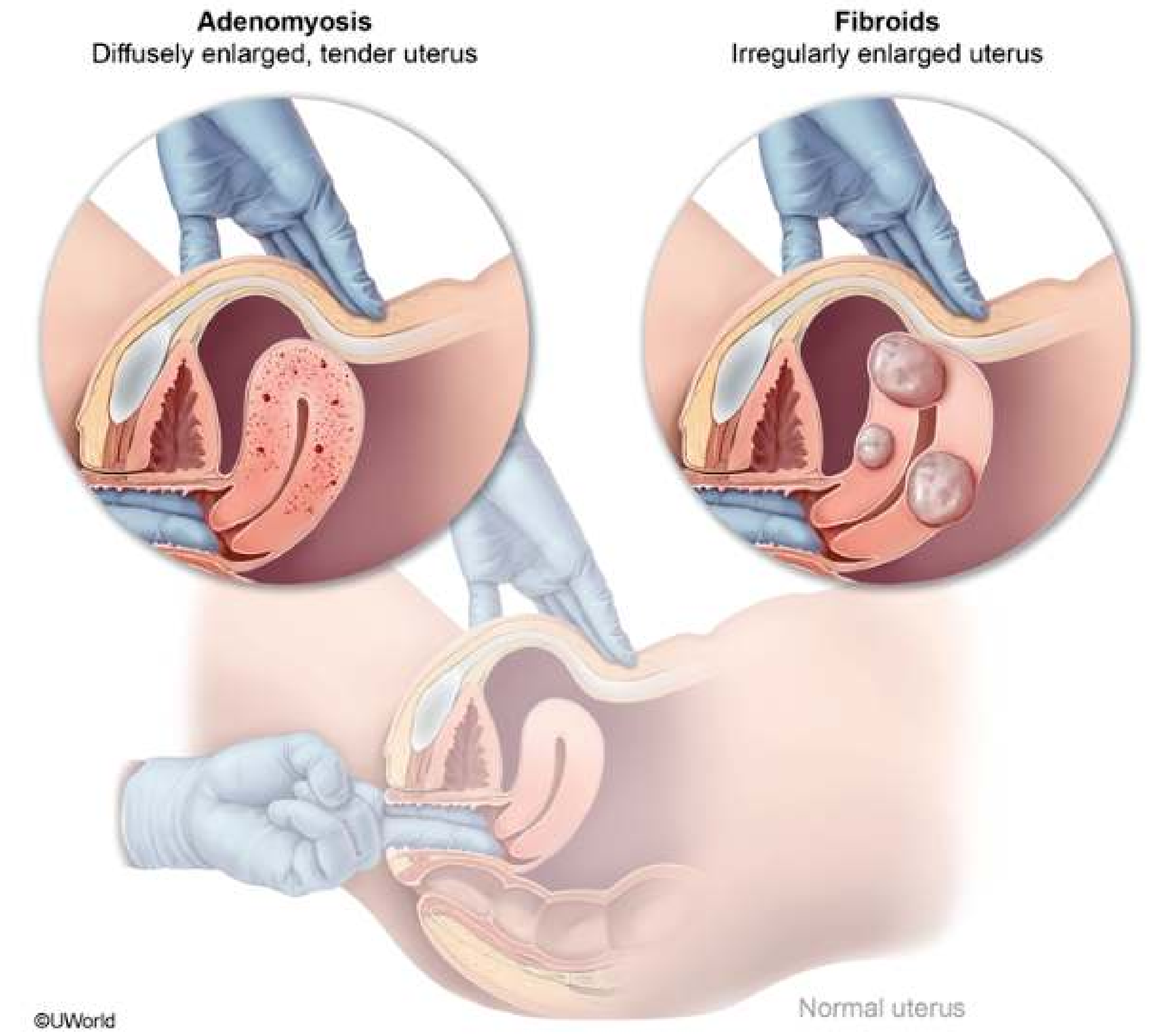
Adenomyosis vs fibroids


Adenomyosis
Diffusely enlarged, tender uterus
Fibroids
Irregularly enlarged uterus
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Normal uterus

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Educational objective:

Adenomyosis is the abnormal presence of endometrial glands and stroma within the uterine myometrium. Affected

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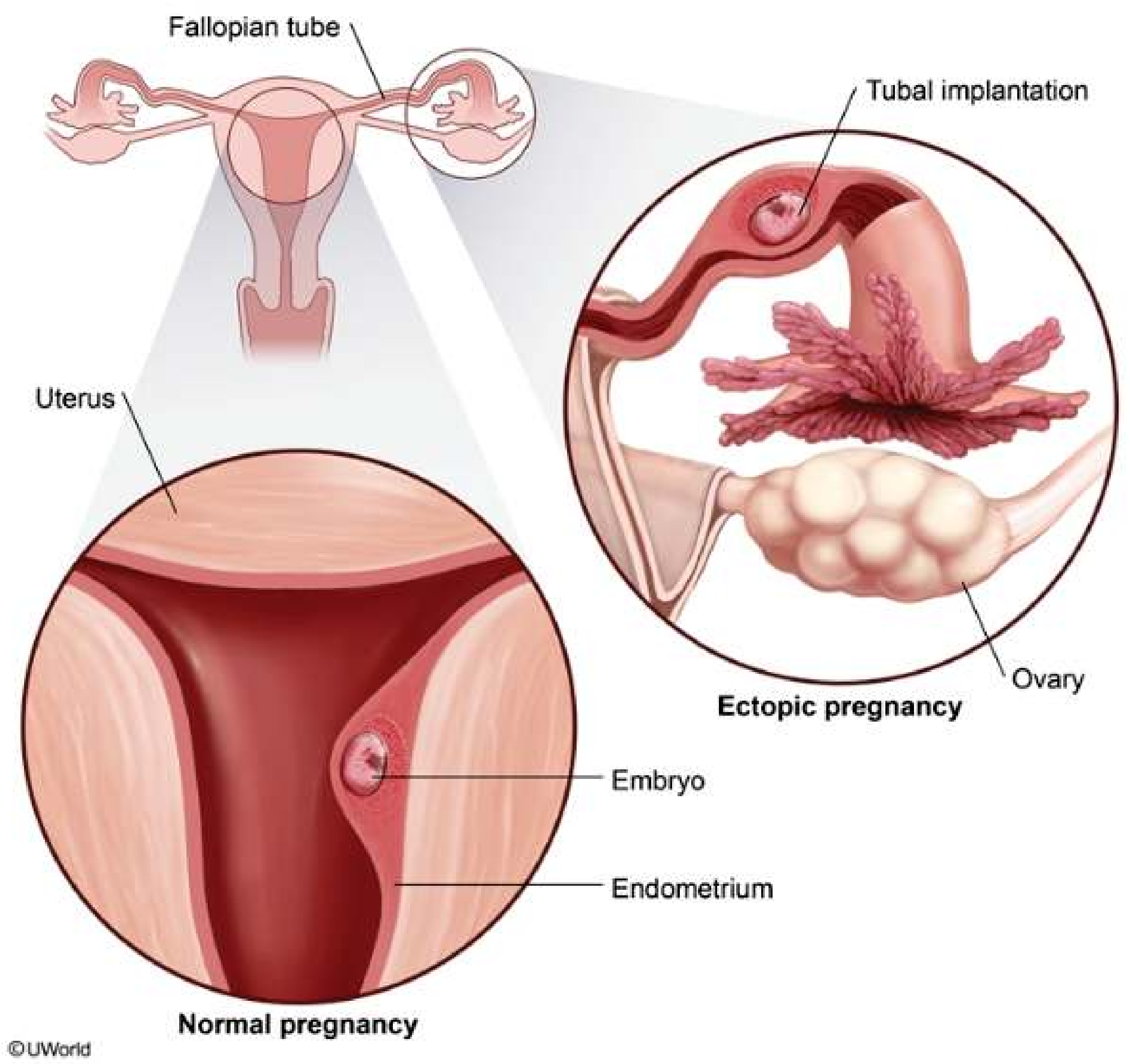
Ectopic pregnancy


Fallopian tube
Tubal implantation
Uterus
Ovary
Ectopic pregnancy
Embryo
Endometrium
Normal pregnancy
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Educational objective:

Adenomyosis is the abnormal presence of endometrial glands and stroma within the uterine myometrium. Affected

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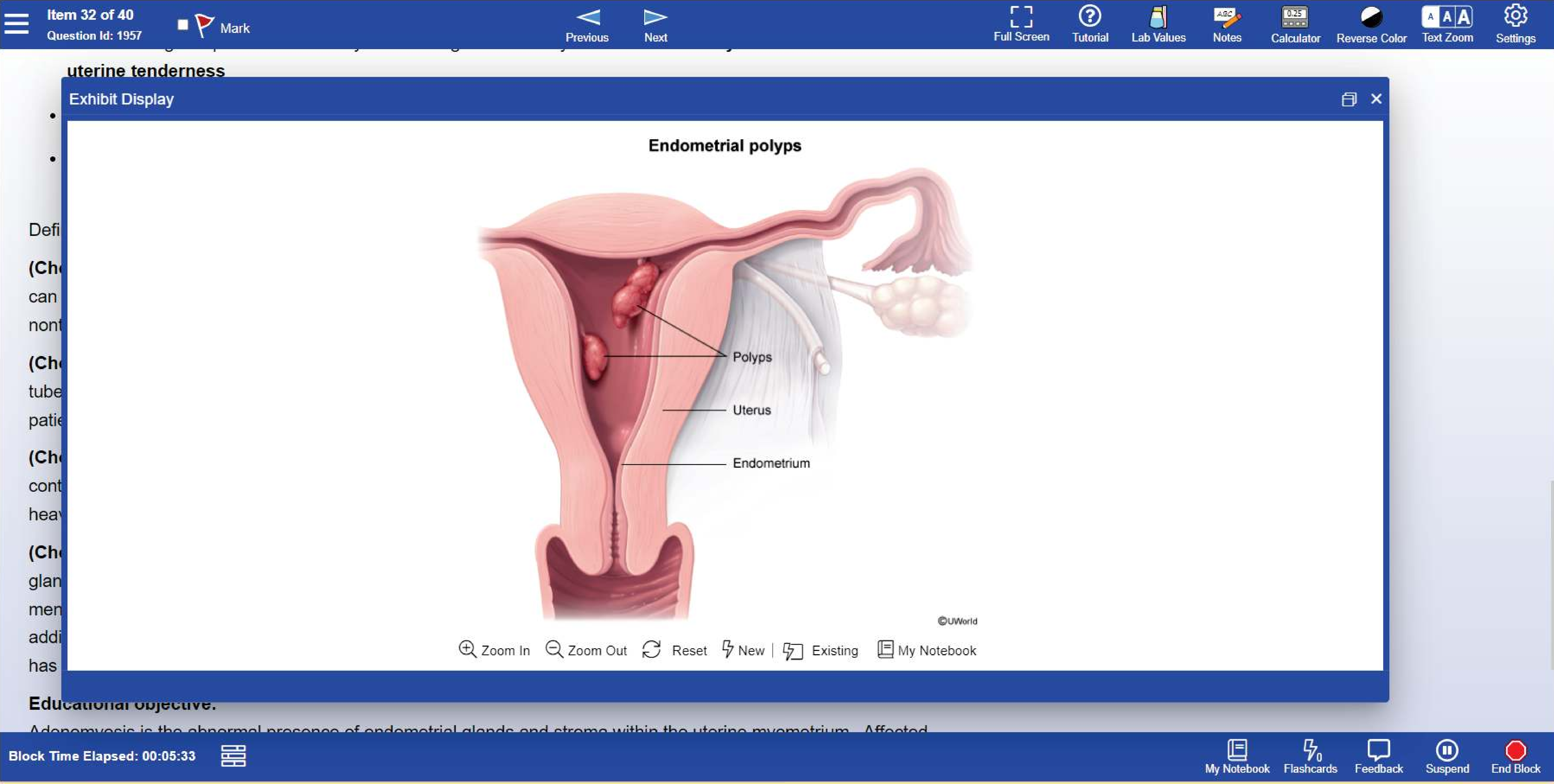
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Endometrial polyps

Educational objective:

Adenomyosis is the abnormal presence of endometrial glands and stroma within the uterine myometrium. Affected

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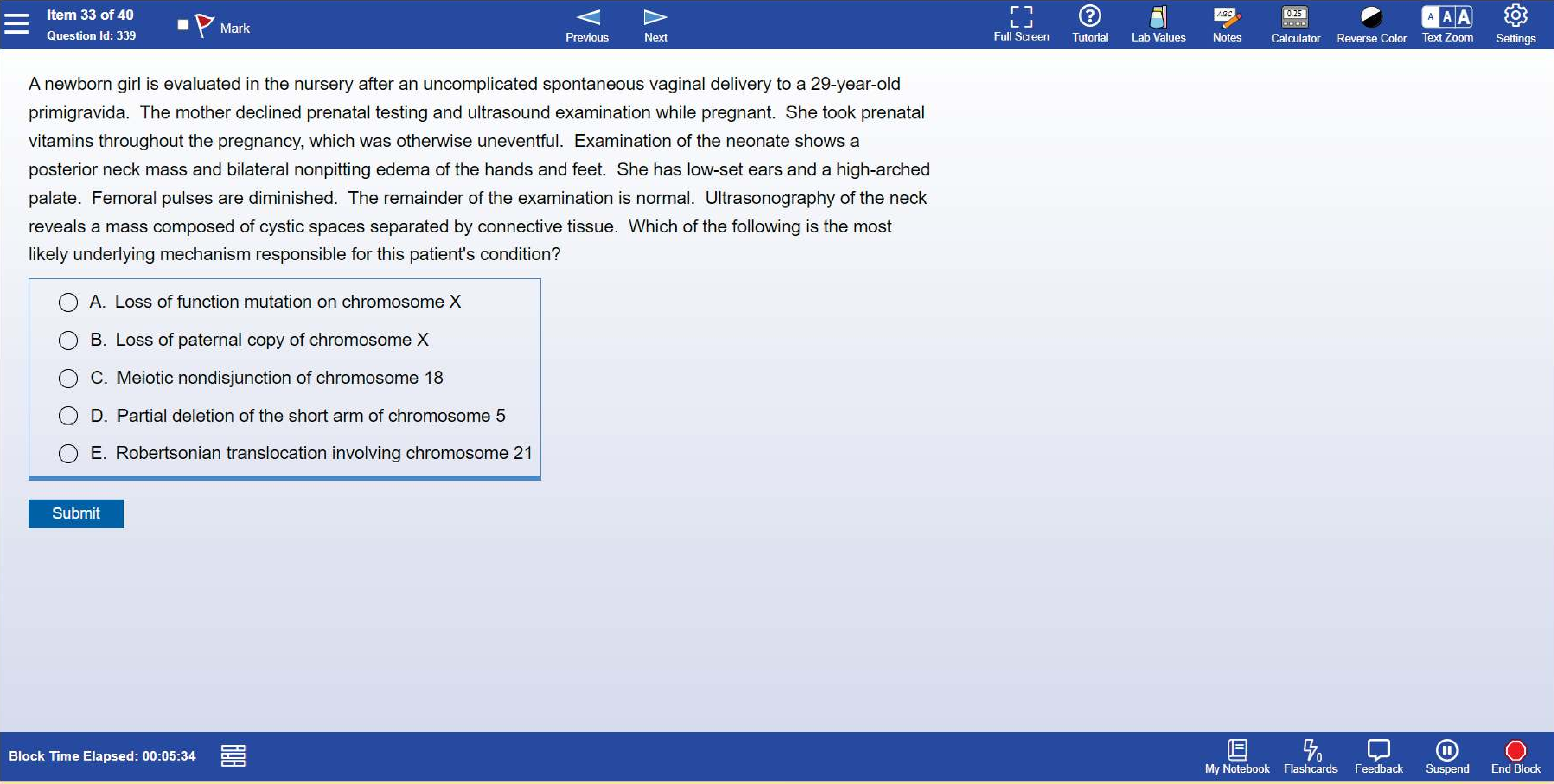
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A newborn girl is evaluated in the nursery after an uncomplicated spontaneous vaginal delivery to a 29-year-old primigravida. The mother declined prenatal testing and ultrasound examination while pregnant. She took prenatal vitamins throughout the pregnancy, which was otherwise uneventful. Examination of the neonate shows a posterior neck mass and bilateral nonpitting edema of the hands and feet. She has low-set ears and a high-arched palate. Femoral pulses are diminished. The remainder of the examination is normal. Ultrasonography of the neck reveals a mass composed of cystic spaces separated by connective tissue. Which of the following is the most likely underlying mechanism responsible for this patient's condition?

○ A. Loss of function mutation on chromosome X
○ B. Loss of paternal copy of chromosome X
○ C. Meiotic nondisjunction of chromosome 18
○ D. Partial deletion of the short arm of chromosome 5
○ E. Robertsonian translocation involving chromosome 21

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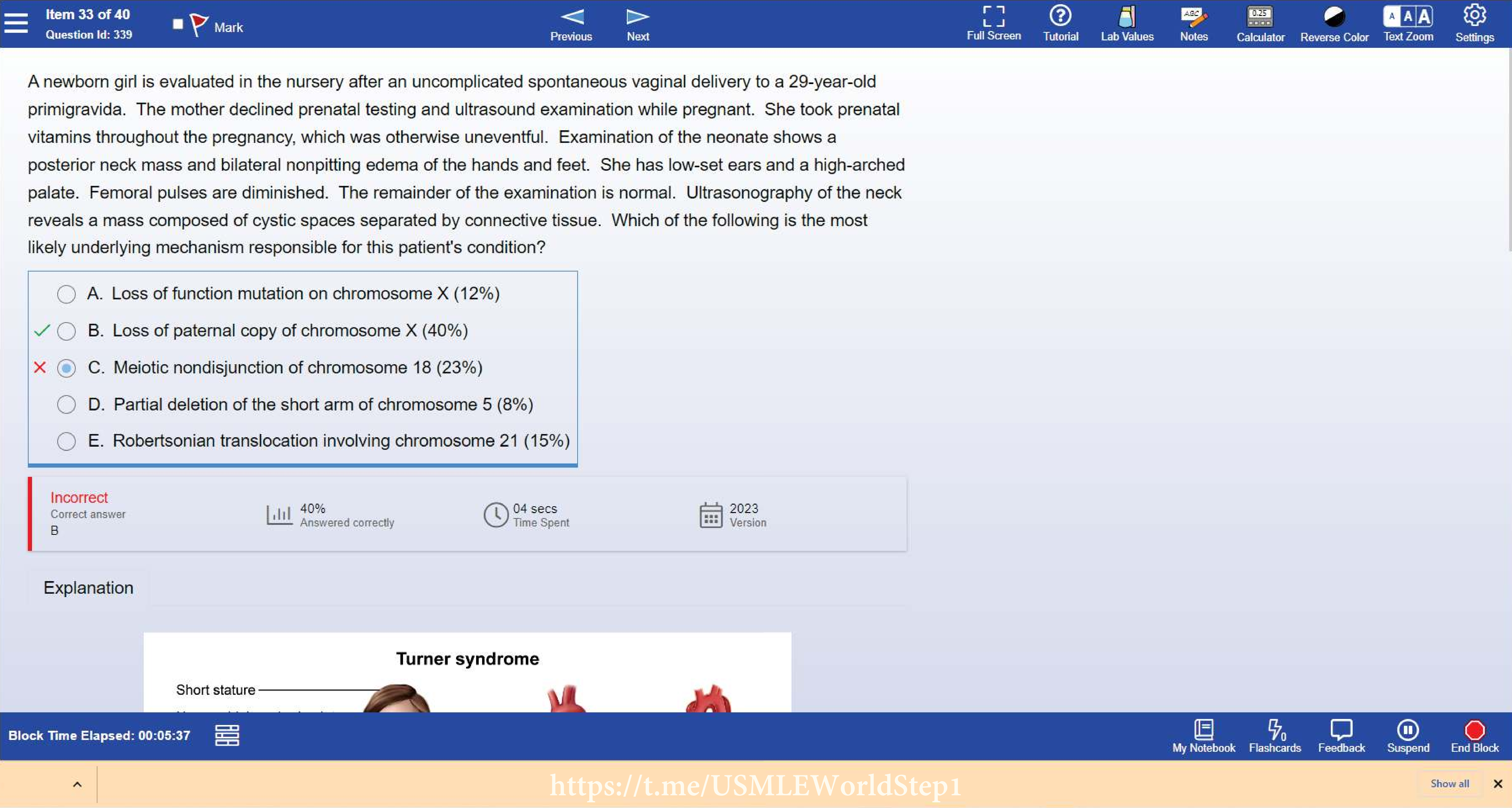
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- ○ A. Loss of function mutation on chromosome X (12%)
- ✓ ○ B. Loss of paternal copy of chromosome X (40%)
- ✗ ● C. Meiotic nondisjunction of chromosome 18 (23%)
- ○ D. Partial deletion of the short arm of chromosome 5 (8%)
- ○ E. Robertsonian translocation involving chromosome 21 (15%)

Incorrect Correct answer B	40% Answered correctly	04 secs Time Spent	2023 Version

Explanation

Turner syndrome

Short stature

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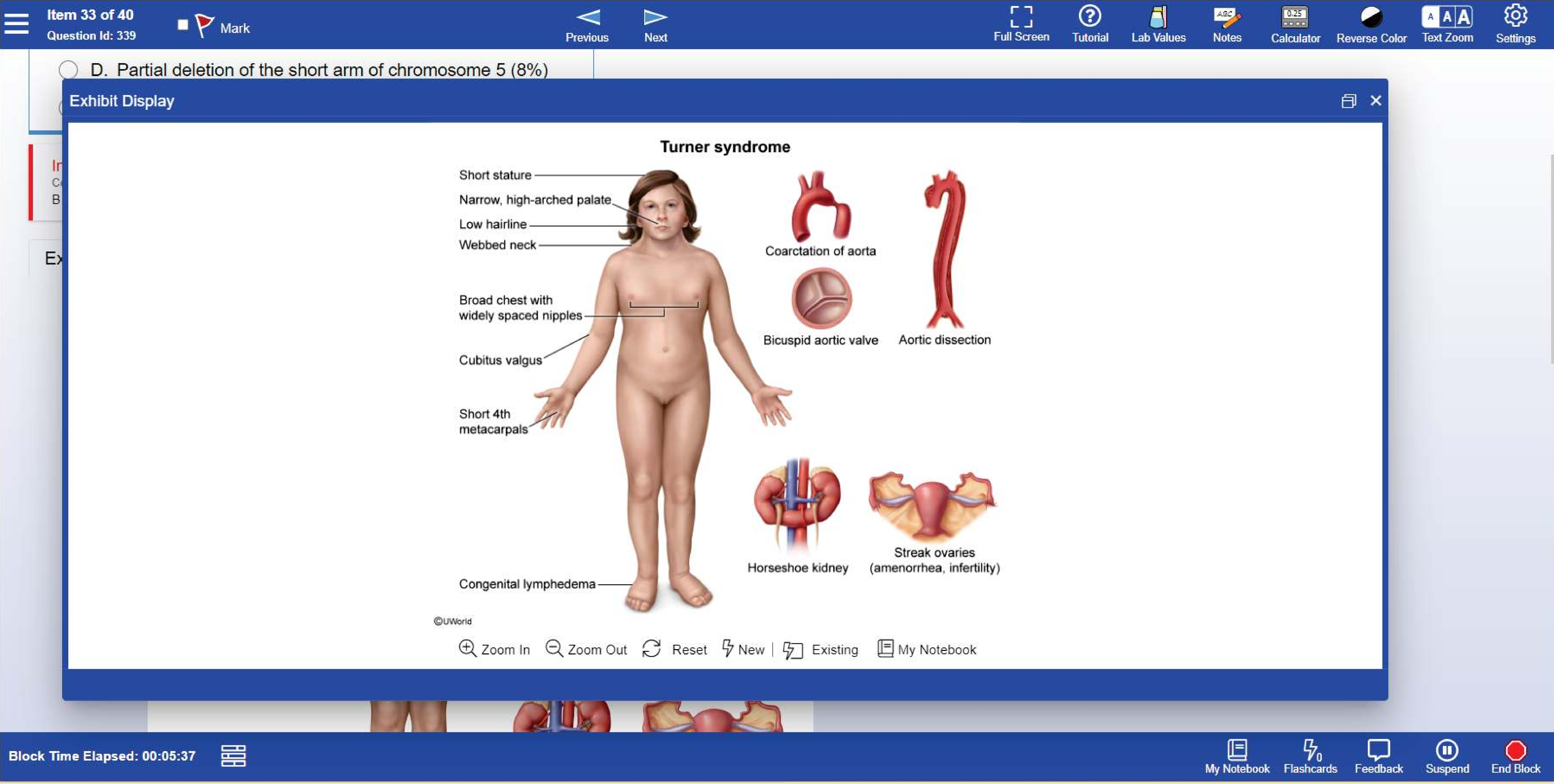
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○ D. Partial deletion of the short arm of chromosome 5 (8%)

Turner syndrome

Short stature
Narrow, high-arched palate
Low hairline
Webbed neck
Broad chest with widely spaced nipples
Cubitus valgus
Short 4th metacarpals
Congenital lymphedema
Coarctation of aorta
Bicuspid aortic valve
Aortic dissection
Horseshoe kidney
Streak ovaries (amenorrhea, infertility)

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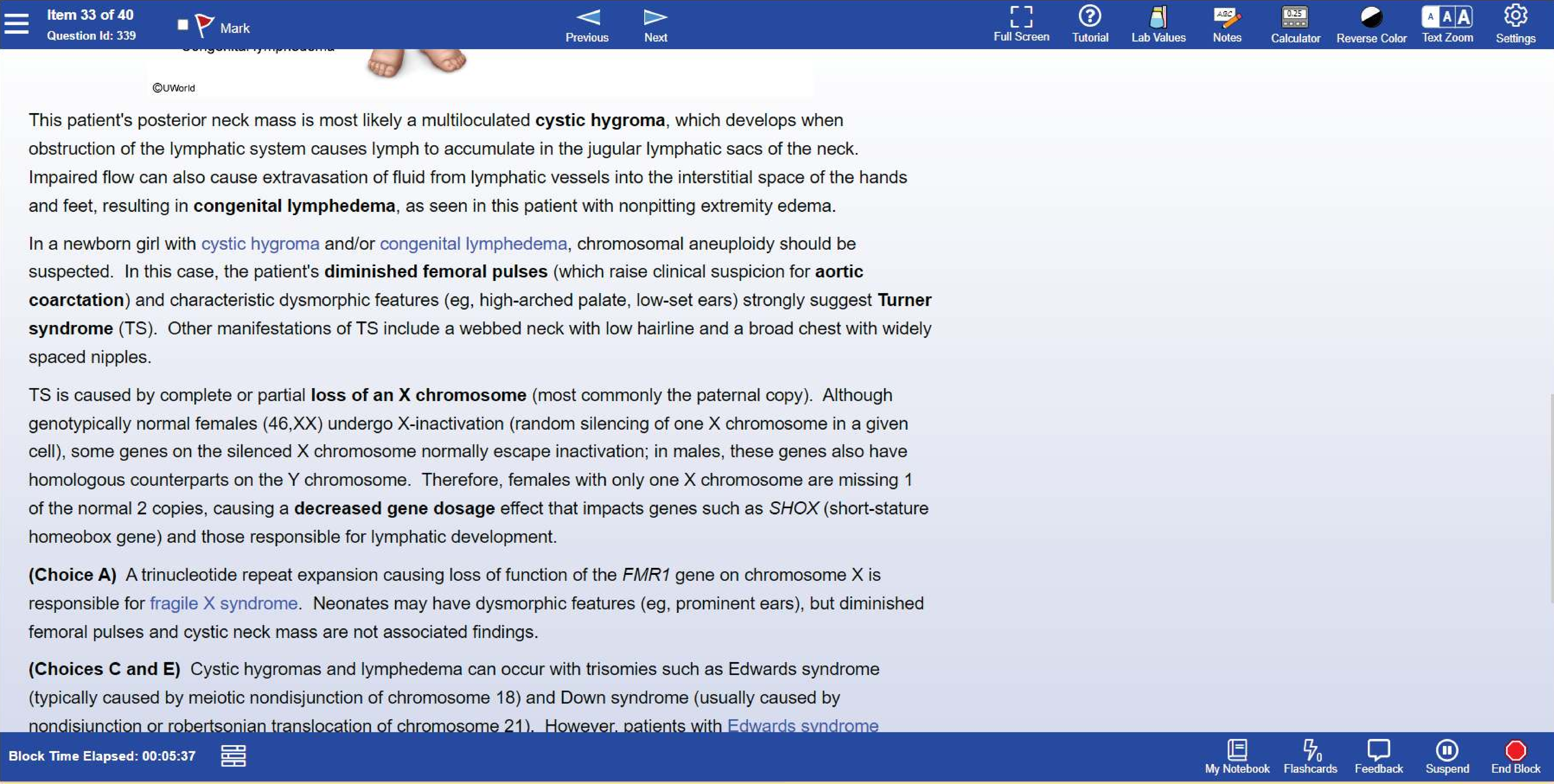
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Congenital lymphedema
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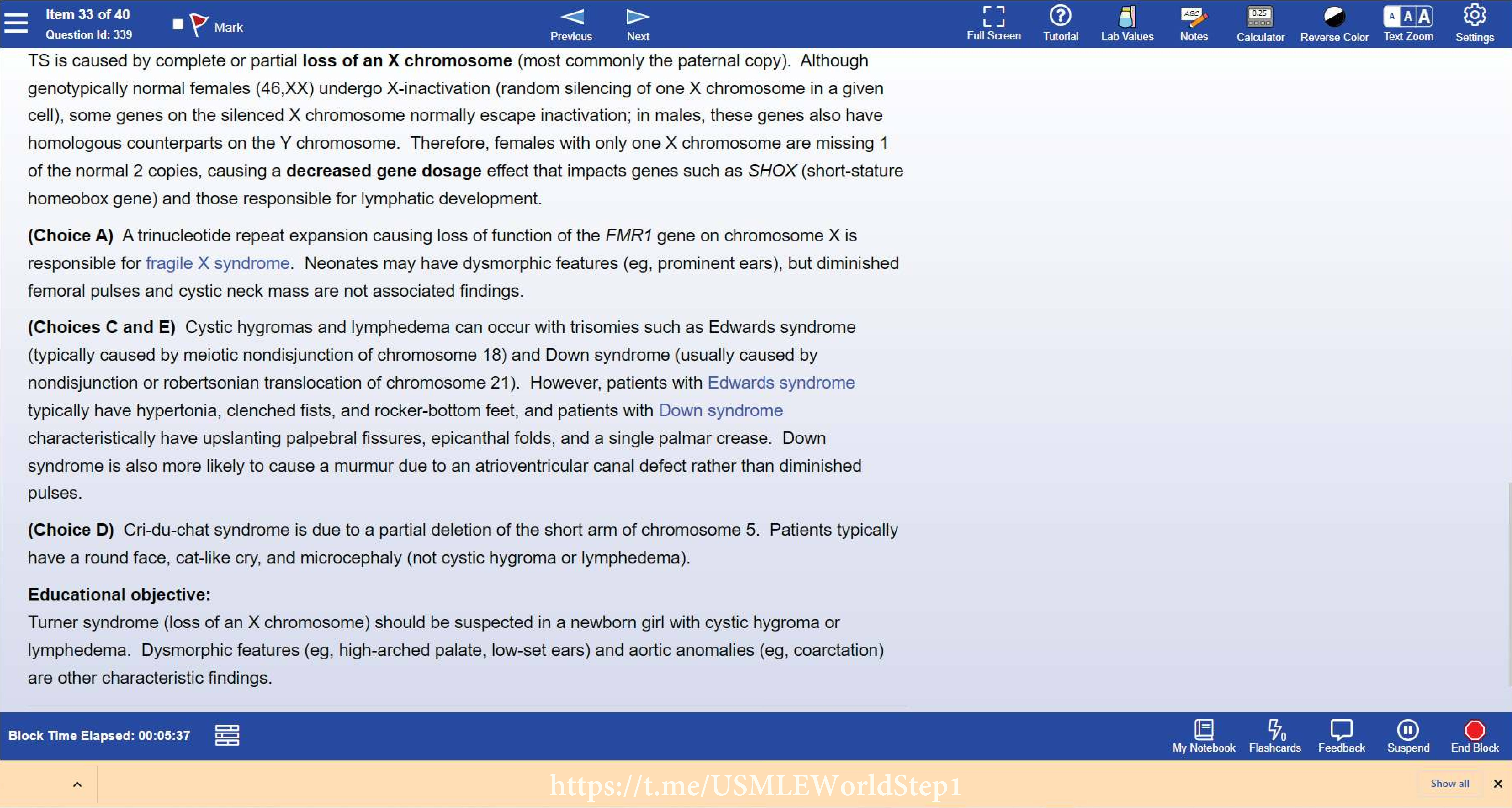
This patient's posterior neck mass is most likely a multiloculated **cystic hygroma**, which develops when obstruction of the lymphatic system causes lymph to accumulate in the jugular lymphatic sacs of the neck. Impaired flow can also cause extravasation of fluid from lymphatic vessels into the interstitial space of the hands and feet, resulting in **congenital lymphedema**, as seen in this patient with nonpitting extremity edema.

In a newborn girl with cystic hygroma and/or congenital lymphedema, chromosomal aneuploidy should be suspected. In this case, the patient's **diminished femoral pulses** (which raise clinical suspicion for **aortic coarctation**) and characteristic dysmorphic features (eg, high-arched palate, low-set ears) strongly suggest **Turner syndrome** (TS). Other manifestations of TS include a webbed neck with low hairline and a broad chest with widely spaced nipples.

TS is caused by complete or partial **loss of an X chromosome** (most commonly the paternal copy). Although genotypically normal females (46,XX) undergo X-inactivation (random silencing of one X chromosome in a given cell), some genes on the silenced X chromosome normally escape inactivation; in males, these genes also have homologous counterparts on the Y chromosome. Therefore, females with only one X chromosome are missing 1 of the normal 2 copies, causing a **decreased gene dosage** effect that impacts genes such as *SHOX* (short-stature homeobox gene) and those responsible for lymphatic development.

(Choice A) A trinucleotide repeat expansion causing loss of function of the *FMR1* gene on chromosome X is responsible for fragile X syndrome. Neonates may have dysmorphic features (eg, prominent ears), but diminished femoral pulses and cystic neck mass are not associated findings.

(Choices C and E) Cystic hygromas and lymphedema can occur with trisomies such as Edwards syndrome (typically caused by meiotic nondisjunction of chromosome 18) and Down syndrome (usually caused by nondisjunction or robertsonian translocation of chromosome 21). However, patients with Edwards syndrome



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(Choices C and E) Cystic hygromas and lymphedema can occur with trisomies such as Edwards syndrome (typically caused by meiotic nondisjunction of chromosome 18) and Down syndrome (usually caused by nondisjunction or robertsonian translocation of chromosome 21). However, patients with Edwards syndrome typically have hypertonia, clenched fists, and rocker-bottom feet, and patients with Down syndrome characteristically have upslanting palpebral fissures, epicanthal folds, and a single palmar crease. Down syndrome is also more likely to cause a murmur due to an atrioventricular canal defect rather than diminished pulses.

(Choice D) Cri-du-chat syndrome is due to a partial deletion of the short arm of chromosome 5. Patients typically have a round face, cat-like cry, and microcephaly (not cystic hygroma or lymphedema).

Educational objective:
Turner syndrome (loss of an X chromosome) should be suspected in a newborn girl with cystic hygroma or lymphedema. Dysmorphic features (eg, high-arched palate, low-set ears) and aortic anomalies (eg, coarctation) are other characteristic findings.

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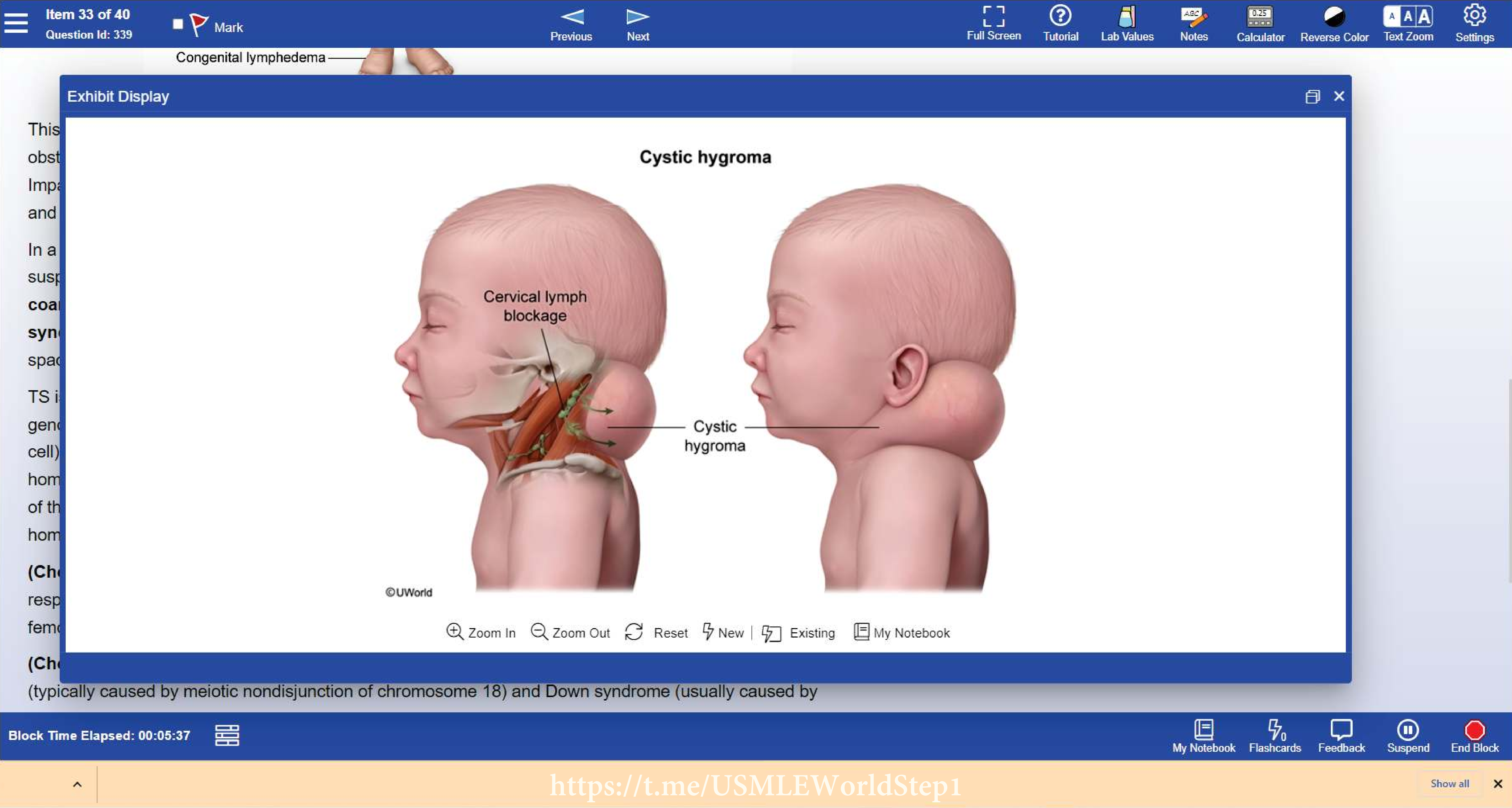
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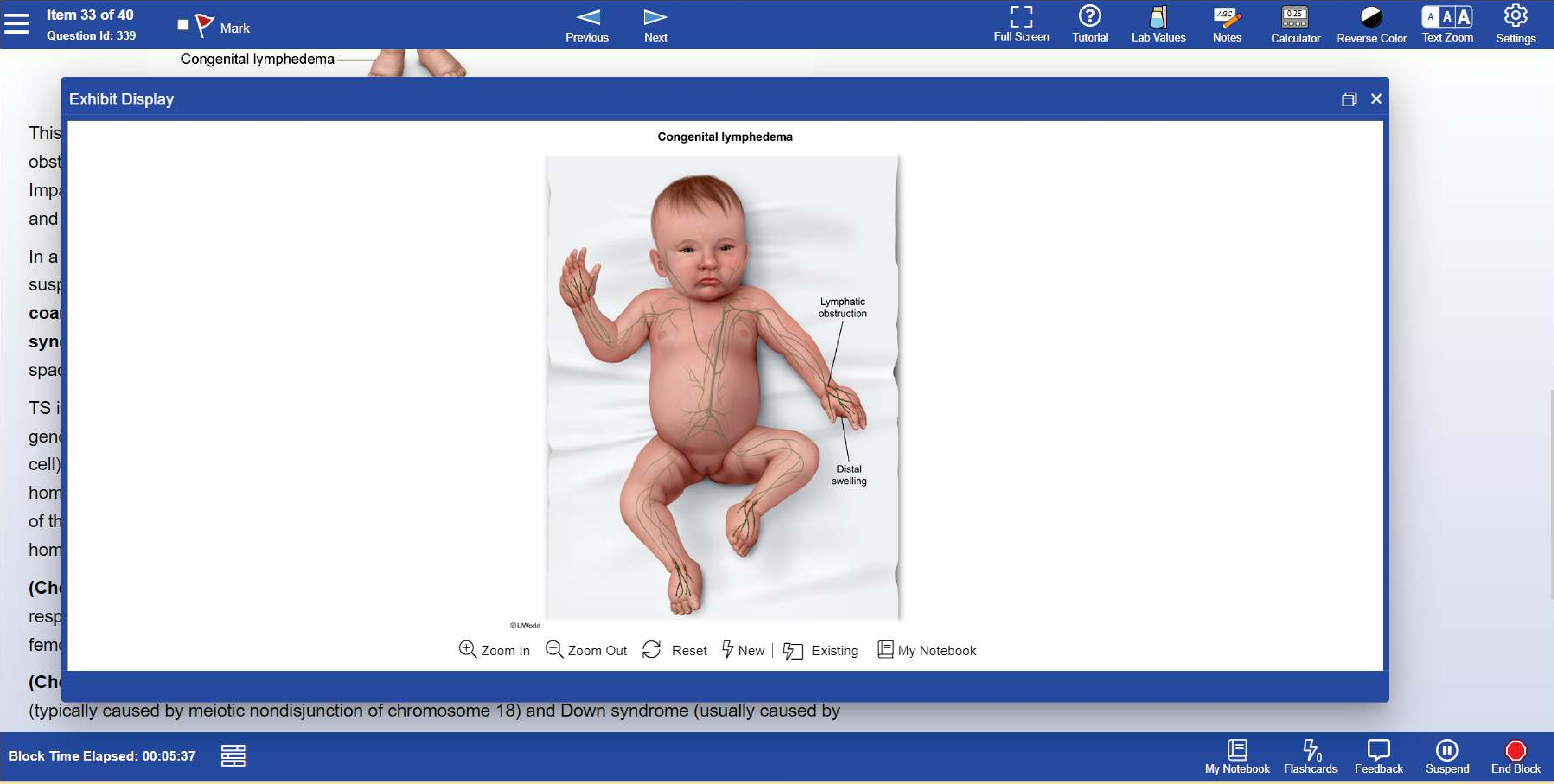
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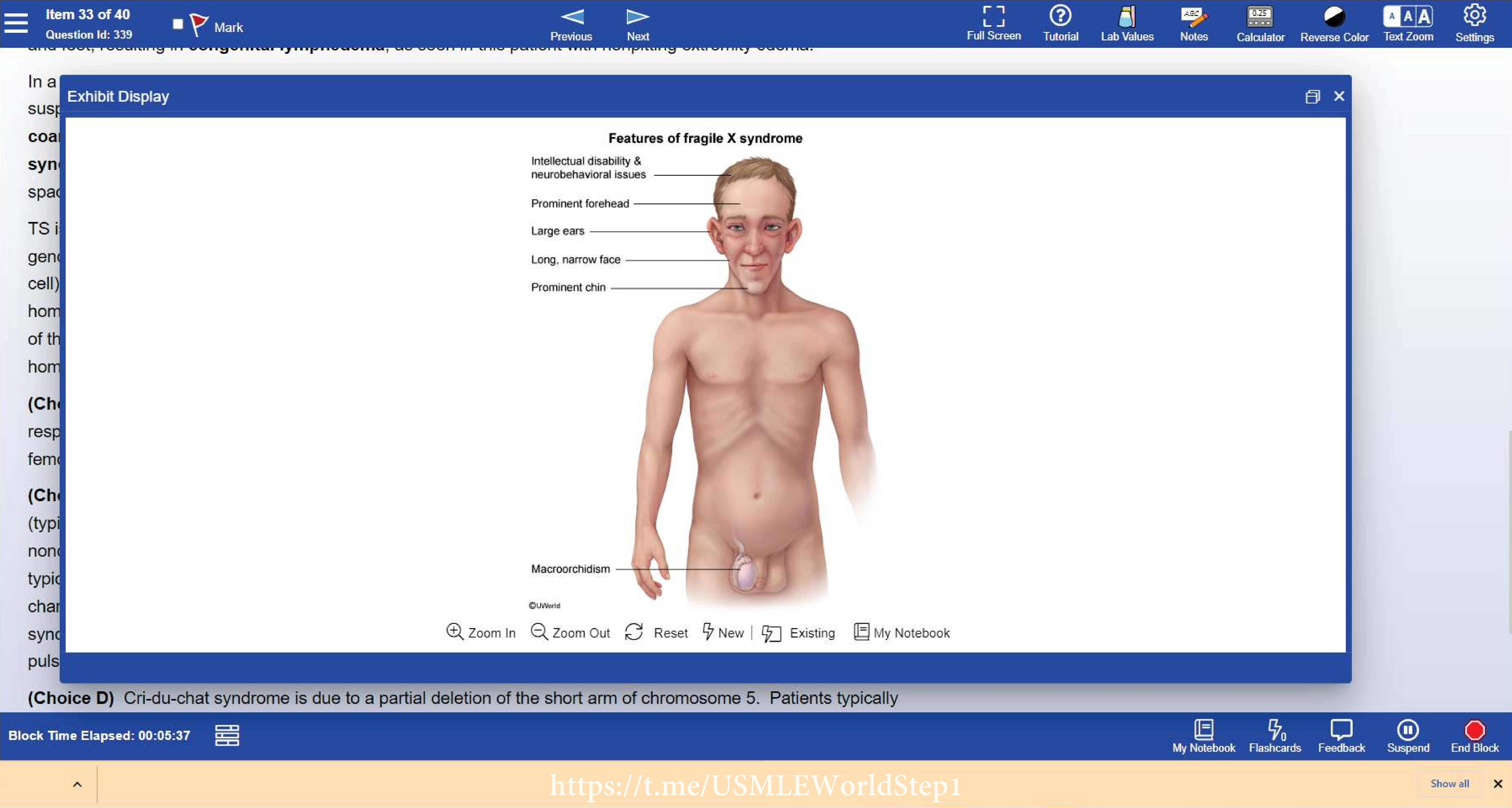
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and feet, resulting in **congenital lymphedema**, as seen in this patient with nonpitting extremity edema.

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Features of fragile X syndrome

Intellectual disability & neurobehavioral issues
Prominent forehead
Large ears
Long, narrow face
Prominent chin
Macroorchidism
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(Choice D) Cri-du-chat syndrome is due to a partial deletion of the short arm of chromosome 5. Patients typically

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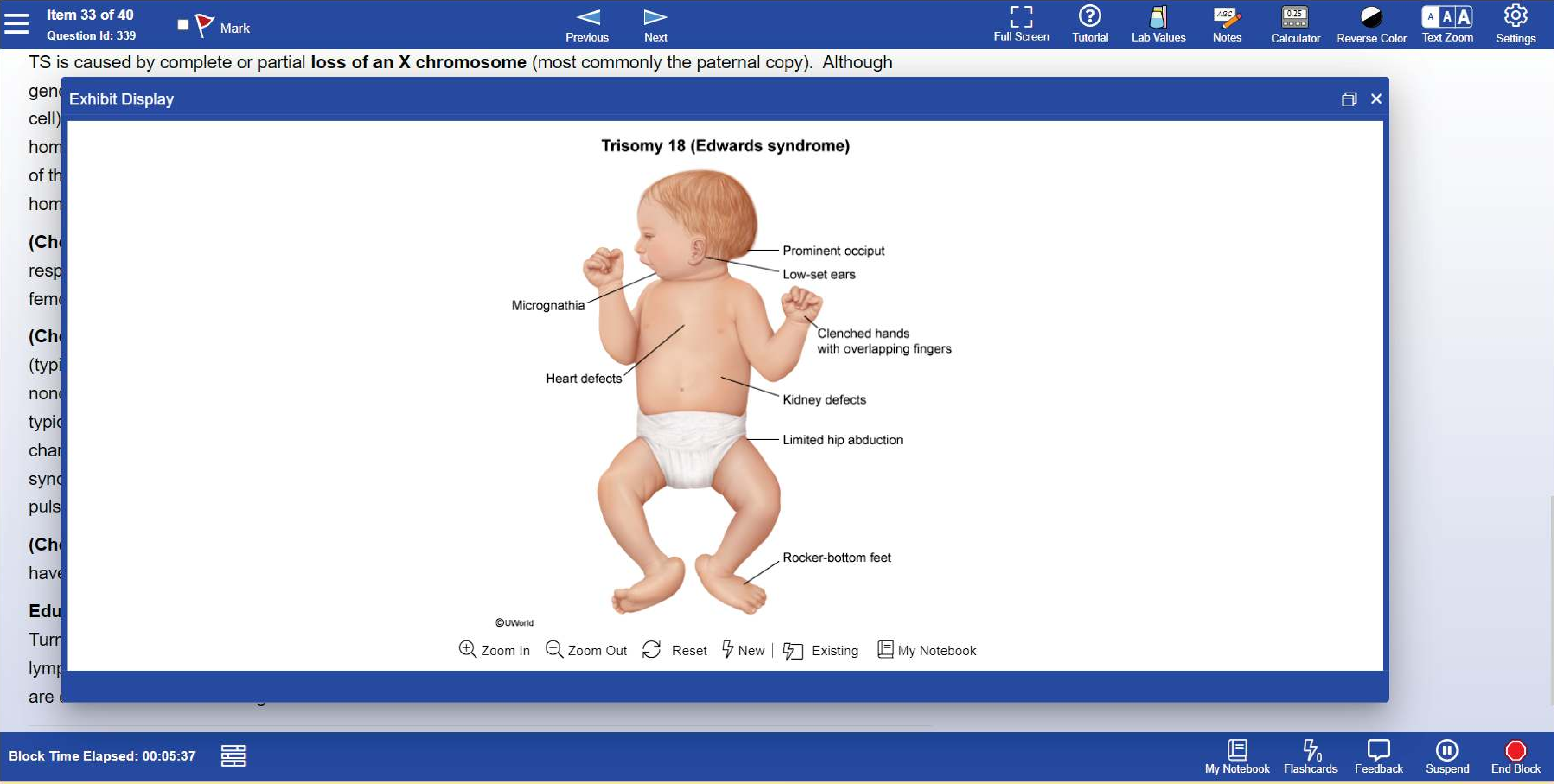
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TS is caused by complete or partial **loss of an X chromosome** (most commonly the paternal copy). Although

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Trisomy 18 (Edwards syndrome)

Prominent occiput
Low-set ears
Micrognathia
Clenched hands with overlapping fingers
Heart defects
Kidney defects
Limited hip abduction
Rocker-bottom feet
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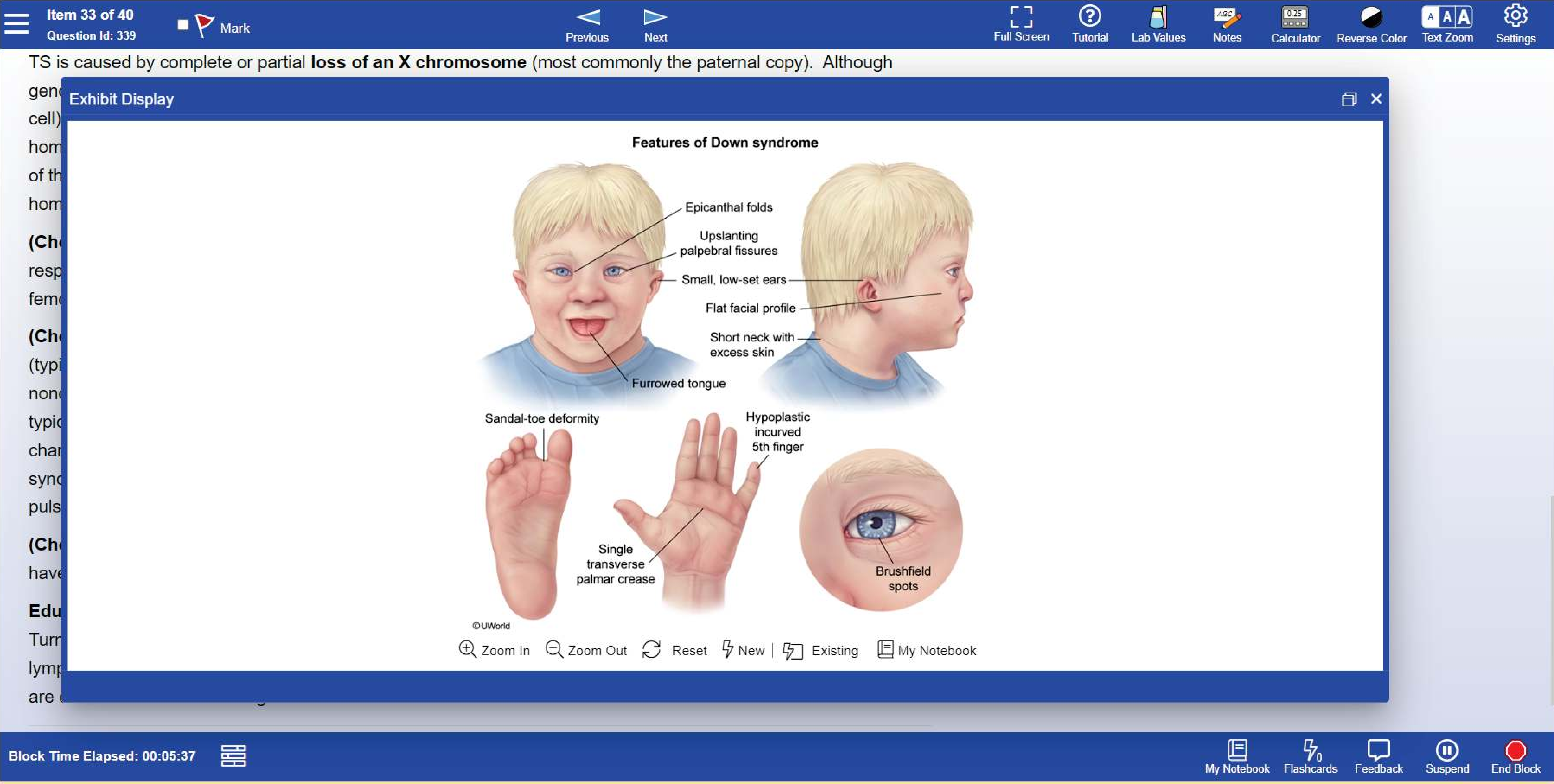
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Features of Down syndrome

Epicanthal folds
Upslanting palpebral fissures
Small, low-set ears
Flat facial profile
Short neck with excess skin
Furrowed tongue
Sandal-toe deformity
Hypoplastic incurved 5th finger
Single transverse palmar crease
Brushfield spots
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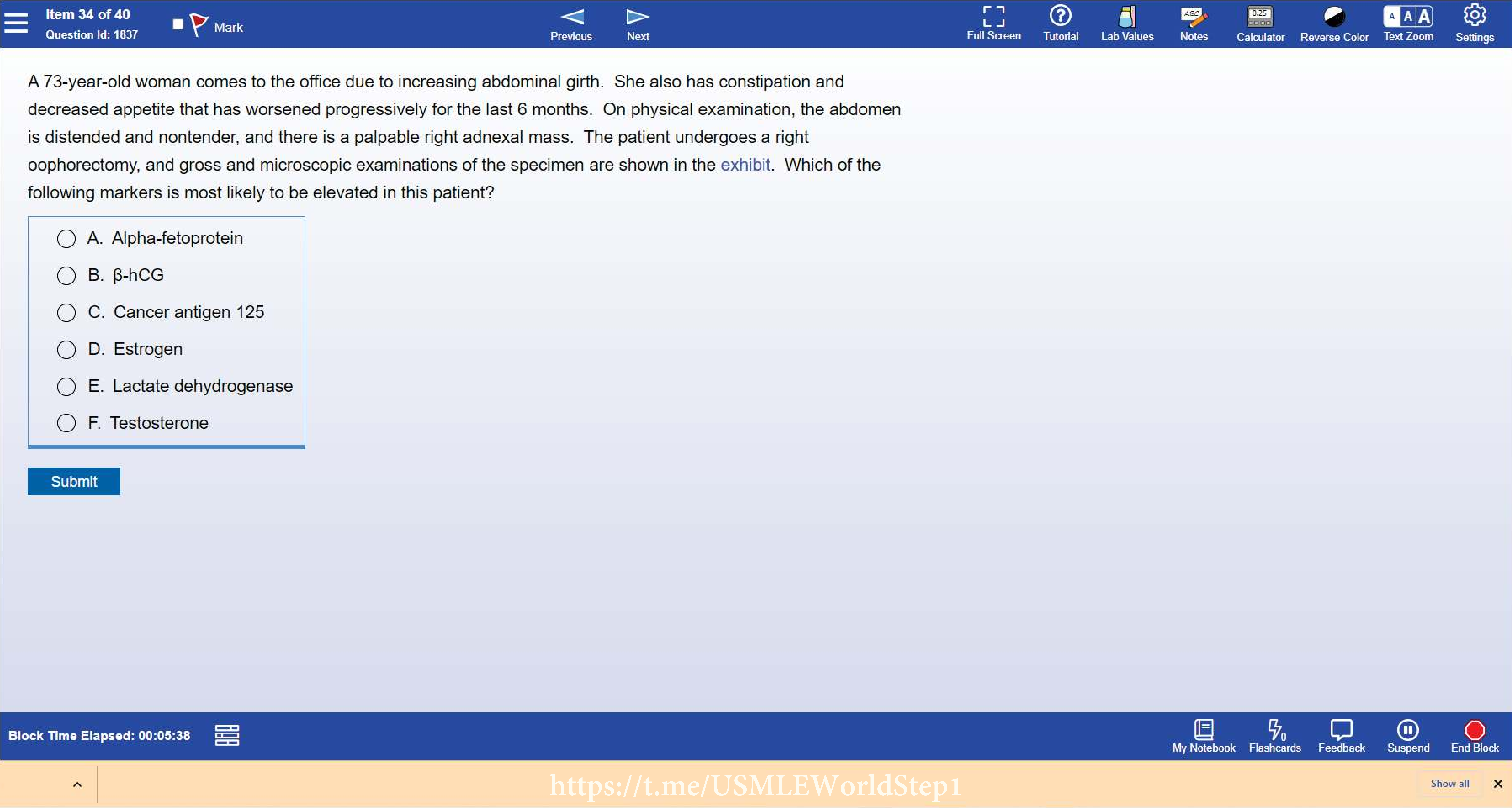
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A 73-year-old woman comes to the office due to increasing abdominal girth. She also has constipation and decreased appetite that has worsened progressively for the last 6 months. On physical examination, the abdomen is distended and nontender, and there is a palpable right adnexal mass. The patient undergoes a right oophorectomy, and gross and microscopic examinations of the specimen are shown in the exhibit. Which of the following markers is most likely to be elevated in this patient?

- ○ A. Alpha-fetoprotein
- ○ B. β-hCG
- ○ C. Cancer antigen 125
- ○ D. Estrogen
- ○ E. Lactate dehydrogenase
- ○ F. Testosterone

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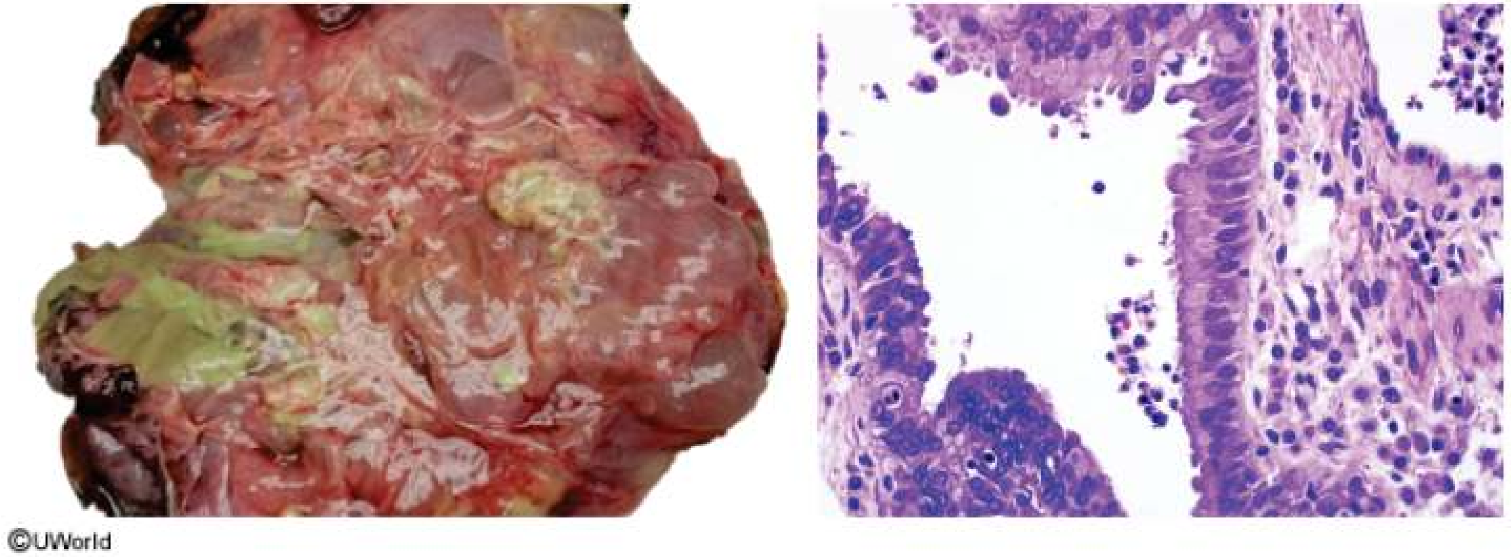

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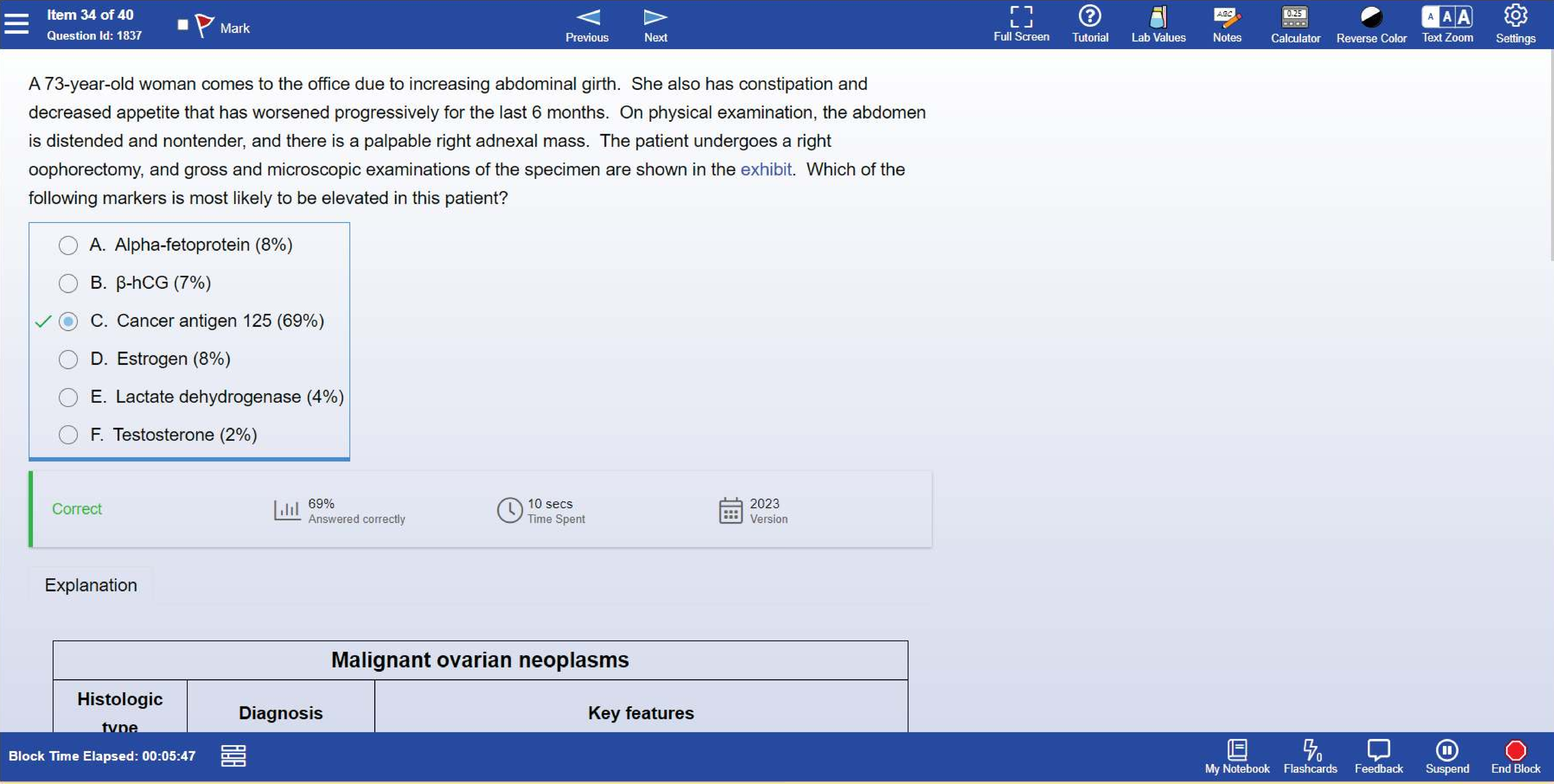
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A 73-year-old woman comes to the office due to increasing abdominal girth. She also has constipation and decreased appetite that has worsened progressively for the last 6 months. On physical examination, the abdomen is distended and nontender, and there is a palpable right adnexal mass. The patient undergoes a right oophorectomy, and gross and microscopic examinations of the specimen are shown in the exhibit. Which of the following markers is most likely to be elevated in this patient?

○ A. Alpha-fetoprotein (8%)
○ B. β-hCG (7%)
✓ ● C. Cancer antigen 125 (69%)
○ D. Estrogen (8%)
○ E. Lactate dehydrogenase (4%)
○ F. Testosterone (2%)

Correct

69% Answered correctly

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Explanation

Malignant ovarian neoplasms		
Histologic type	Diagnosis	Key features

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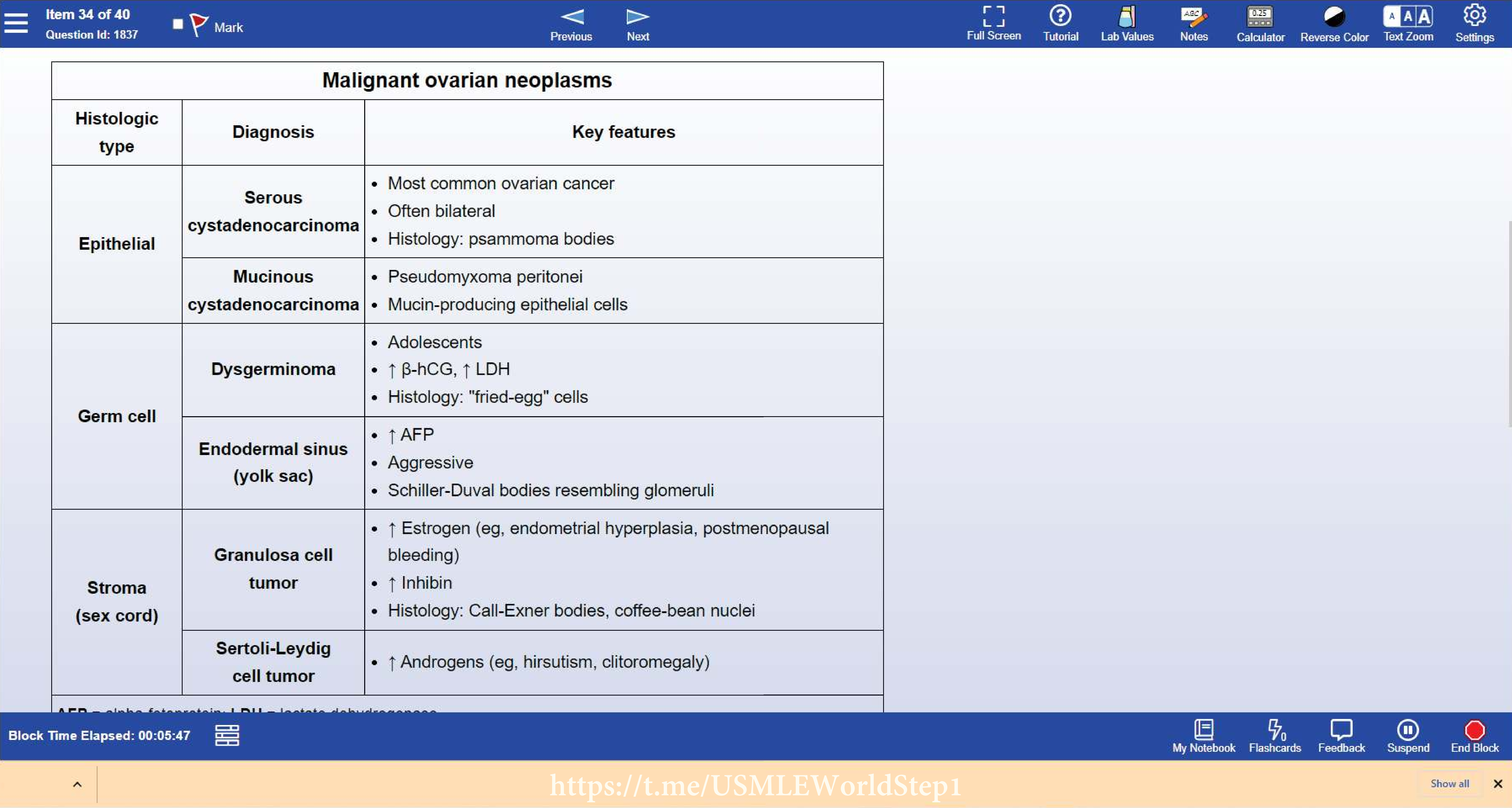
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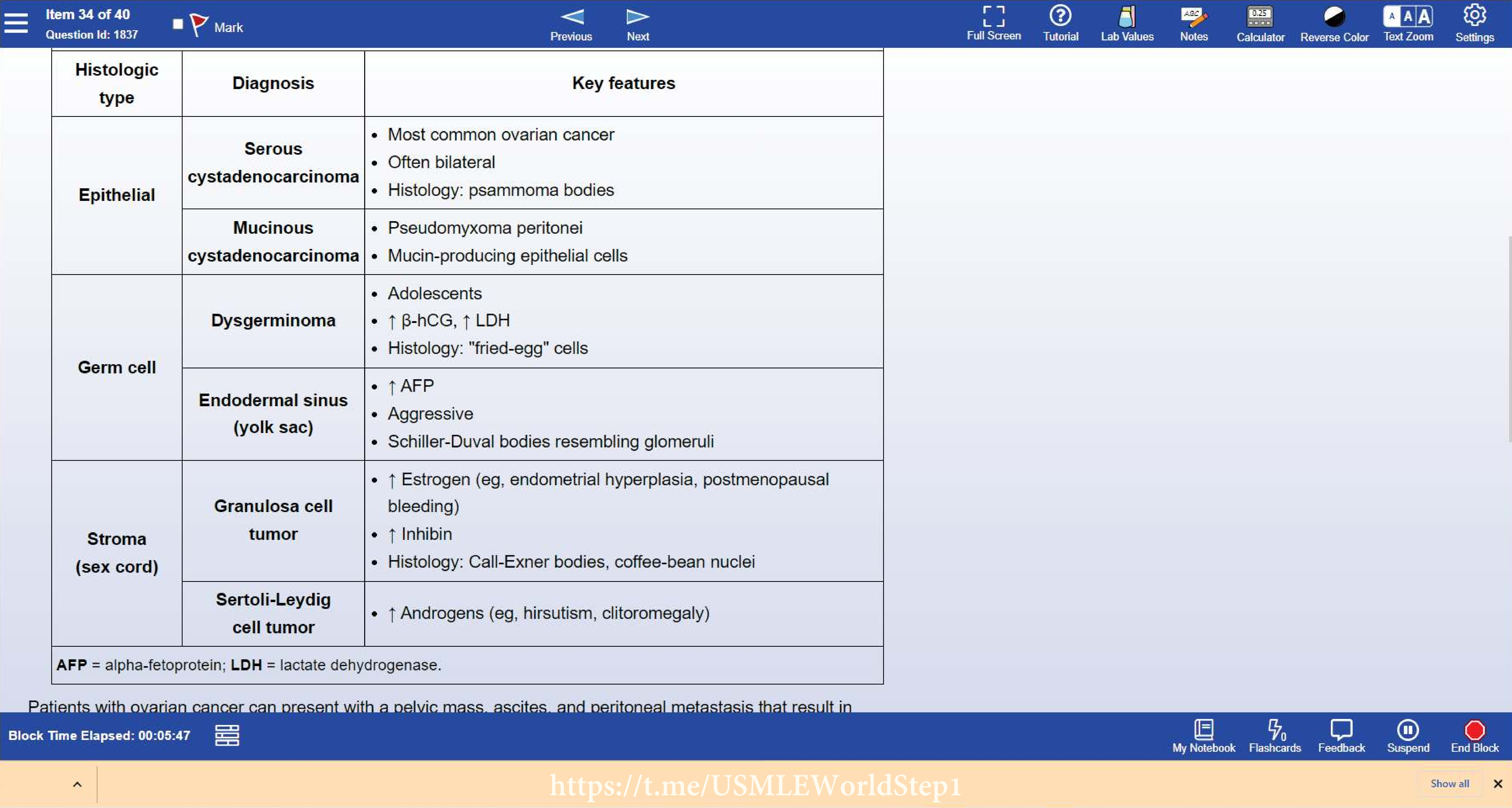
Malignant ovarian neoplasms

Histologic type	Diagnosis	Key features
Epithelial	**Serous cystadenocarcinoma**	• Most common ovarian cancer • Often bilateral • Histology: psammoma bodies
	Mucinous cystadenocarcinoma	• Pseudomyxoma peritonei • Mucin-producing epithelial cells
Germ cell	**Dysgerminoma**	• Adolescents • ↑ β-hCG, ↑ LDH • Histology: "fried-egg" cells
	Endodermal sinus (yolk sac)	• ↑ AFP • Aggressive • Schiller-Duval bodies resembling glomeruli
Stroma (sex cord)	**Granulosa cell tumor**	• ↑ Estrogen (eg, endometrial hyperplasia, postmenopausal bleeding) • ↑ Inhibin • Histology: Call-Exner bodies, coffee-bean nuclei
	Sertoli-Leydig cell tumor	• ↑ Androgens (eg, hirsutism, clitoromegaly)

AFP = alpha-fetoprotein; **LDH** = lactate dehydrogenase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Histologic type	Diagnosis	Key features
Epithelial	**Serous cystadenocarcinoma**	- Most common ovarian cancer - Often bilateral - Histology: psammoma bodies
	Mucinous cystadenocarcinoma	- Pseudomyxoma peritonei - Mucin-producing epithelial cells
Germ cell	**Dysgerminoma**	- Adolescents - ↑ β-hCG, ↑ LDH - Histology: "fried-egg" cells
	Endodermal sinus (yolk sac)	- ↑ AFP - Aggressive - Schiller-Duval bodies resembling glomeruli
Stroma (sex cord)	**Granulosa cell tumor**	- ↑ Estrogen (eg, endometrial hyperplasia, postmenopausal bleeding) - ↑ Inhibin - Histology: Call-Exner bodies, coffee-bean nuclei
	Sertoli-Leydig cell tumor	- ↑ Androgens (eg, hirsutism, clitoromegaly)

AFP = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

Patients with ovarian cancer can present with a pelvic mass, ascites, and peritoneal metastasis that result in

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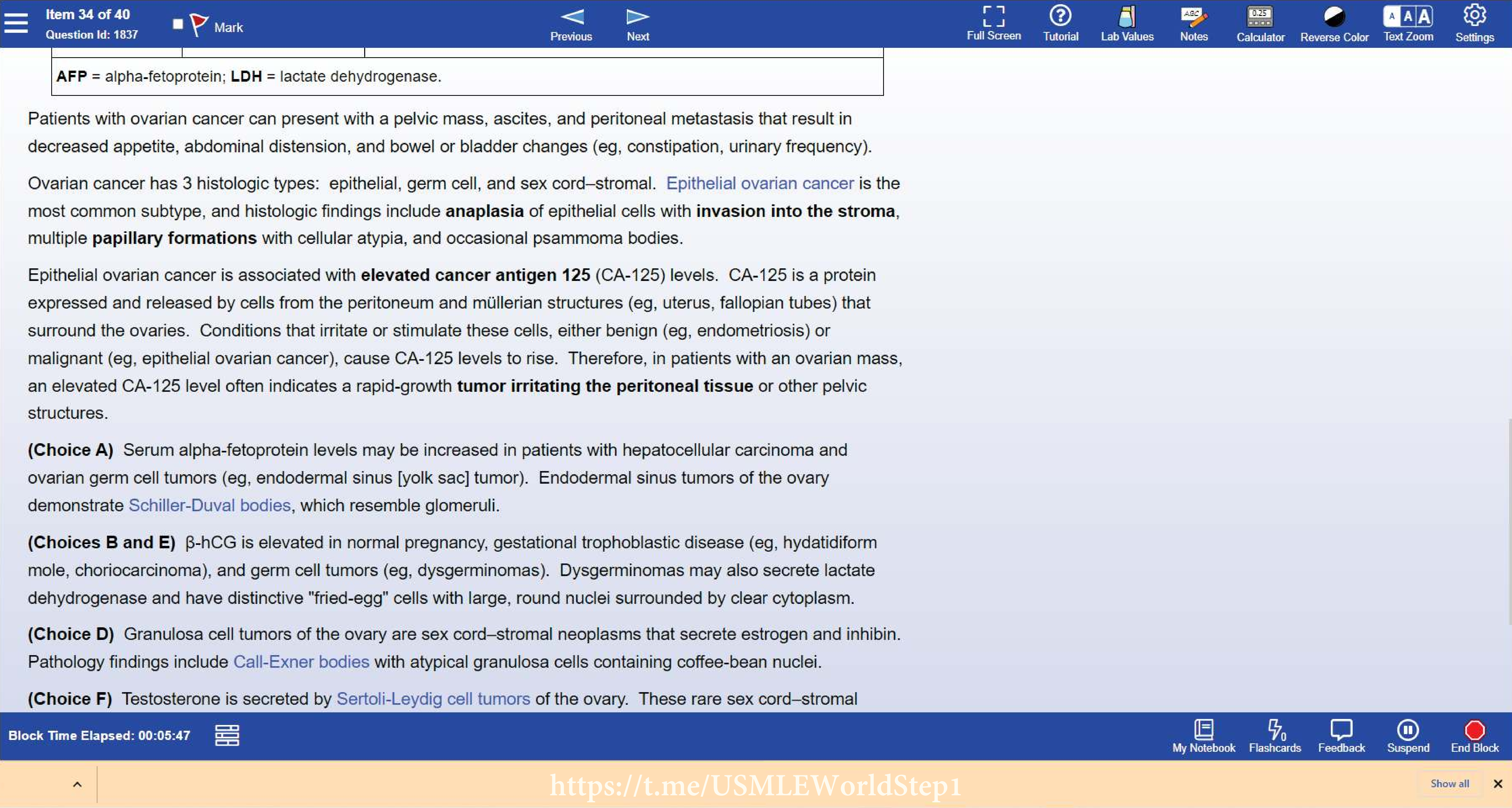

AFP = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

Patients with ovarian cancer can present with a pelvic mass, ascites, and peritoneal metastasis that result in decreased appetite, abdominal distension, and bowel or bladder changes (eg, constipation, urinary frequency).

Ovarian cancer has 3 histologic types: epithelial, germ cell, and sex cord–stromal. Epithelial ovarian cancer is the most common subtype, and histologic findings include **anaplasia** of epithelial cells with **invasion into the stroma**, multiple **papillary formations** with cellular atypia, and occasional psammoma bodies.

Epithelial ovarian cancer is associated with **elevated cancer antigen 125** (CA-125) levels. CA-125 is a protein expressed and released by cells from the peritoneum and müllerian structures (eg, uterus, fallopian tubes) that surround the ovaries. Conditions that irritate or stimulate these cells, either benign (eg, endometriosis) or malignant (eg, epithelial ovarian cancer), cause CA-125 levels to rise. Therefore, in patients with an ovarian mass, an elevated CA-125 level often indicates a rapid-growth **tumor irritating the peritoneal tissue** or other pelvic structures.

(Choice A) Serum alpha-fetoprotein levels may be increased in patients with hepatocellular carcinoma and ovarian germ cell tumors (eg, endodermal sinus [yolk sac] tumor). Endodermal sinus tumors of the ovary demonstrate Schiller-Duval bodies, which resemble glomeruli.

(Choices B and E) β-hCG is elevated in normal pregnancy, gestational trophoblastic disease (eg, hydatidiform mole, choriocarcinoma), and germ cell tumors (eg, dysgerminomas). Dysgerminomas may also secrete lactate dehydrogenase and have distinctive "fried-egg" cells with large, round nuclei surrounded by clear cytoplasm.

(Choice D) Granulosa cell tumors of the ovary are sex cord–stromal neoplasms that secrete estrogen and inhibin. Pathology findings include Call-Exner bodies with atypical granulosa cells containing coffee-bean nuclei.

(Choice F) Testosterone is secreted by Sertoli-Leydig cell tumors of the ovary. These rare sex cord–stromal

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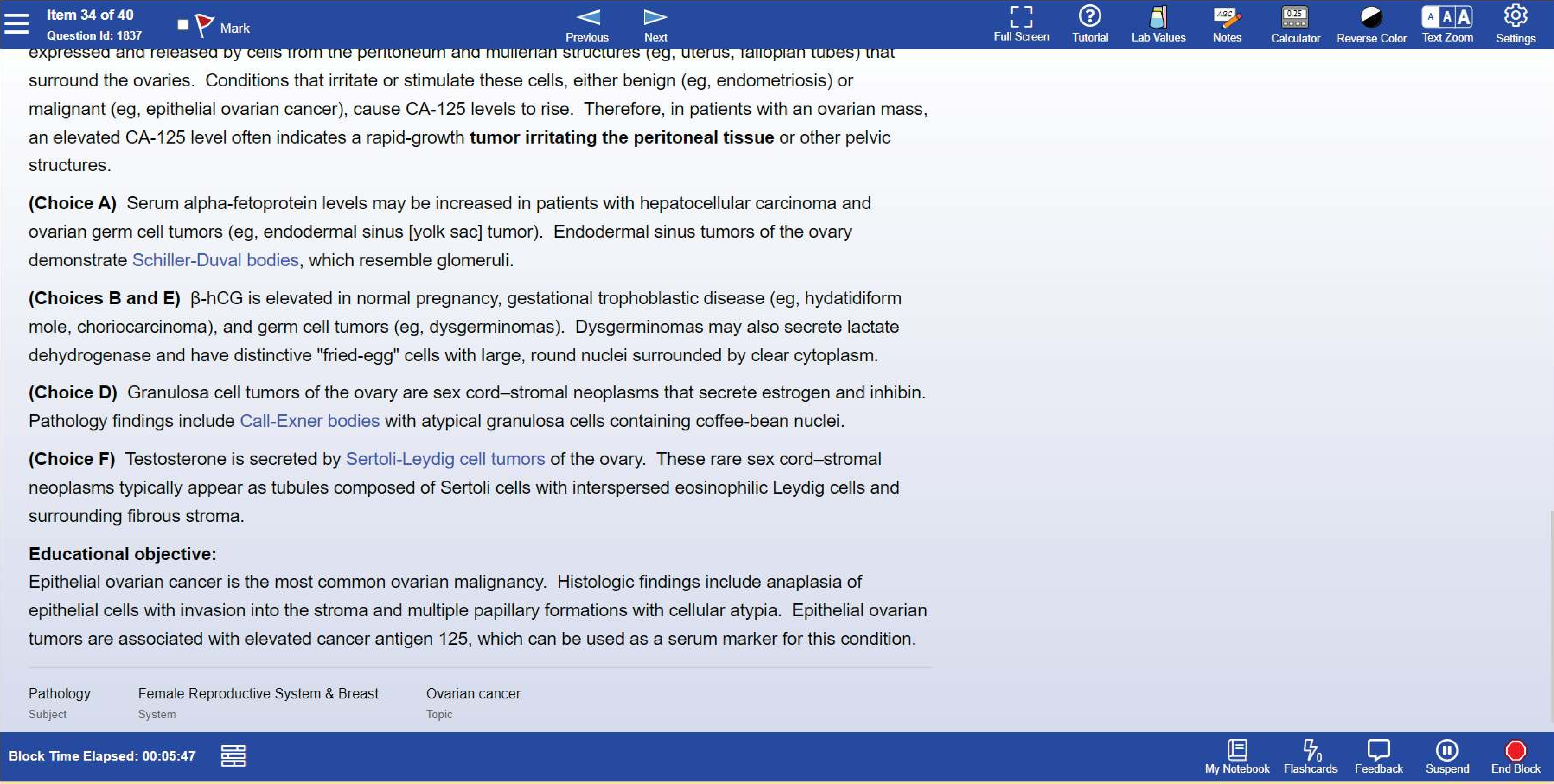
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(Choice A) Serum alpha-fetoprotein levels may be increased in patients with hepatocellular carcinoma and ovarian germ cell tumors (eg, endodermal sinus [yolk sac] tumor). Endodermal sinus tumors of the ovary demonstrate Schiller-Duval bodies, which resemble glomeruli.

(Choices B and E) β-hCG is elevated in normal pregnancy, gestational trophoblastic disease (eg, hydatidiform mole, choriocarcinoma), and germ cell tumors (eg, dysgerminomas). Dysgerminomas may also secrete lactate dehydrogenase and have distinctive "fried-egg" cells with large, round nuclei surrounded by clear cytoplasm.

(Choice D) Granulosa cell tumors of the ovary are sex cord–stromal neoplasms that secrete estrogen and inhibin. Pathology findings include Call-Exner bodies with atypical granulosa cells containing coffee-bean nuclei.

(Choice F) Testosterone is secreted by Sertoli-Leydig cell tumors of the ovary. These rare sex cord–stromal neoplasms typically appear as tubules composed of Sertoli cells with interspersed eosinophilic Leydig cells and surrounding fibrous stroma.

Educational objective:

Epithelial ovarian cancer is the most common ovarian malignancy. Histologic findings include anaplasia of epithelial cells with invasion into the stroma and multiple papillary formations with cellular atypia. Epithelial ovarian tumors are associated with elevated cancer antigen 125, which can be used as a serum marker for this condition.

Pathology	Female Reproductive System & Breast	Ovarian cancer
Subject	System	Topic

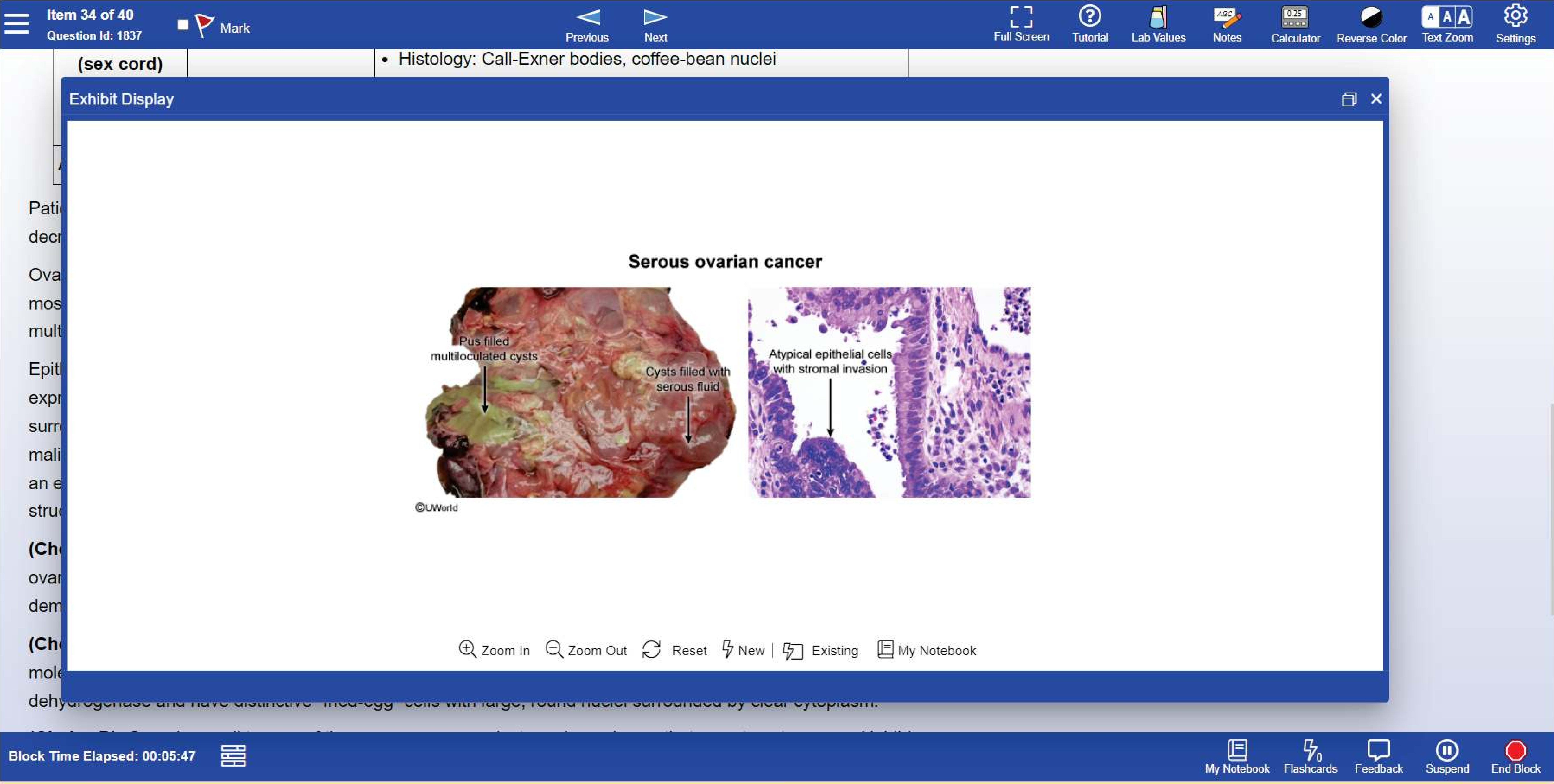
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Exhibit Display
Pus filled multiloculated cysts
Cysts filled with serous fluid
Atypical epithelial cells with stromal invasion
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(sex cord)

- Histology: Call-Exner bodies, coffee-bean nuclei

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Serous ovarian cancer

(sex cord)

- Histology: Call-Exner bodies, coffee-bean nuclei

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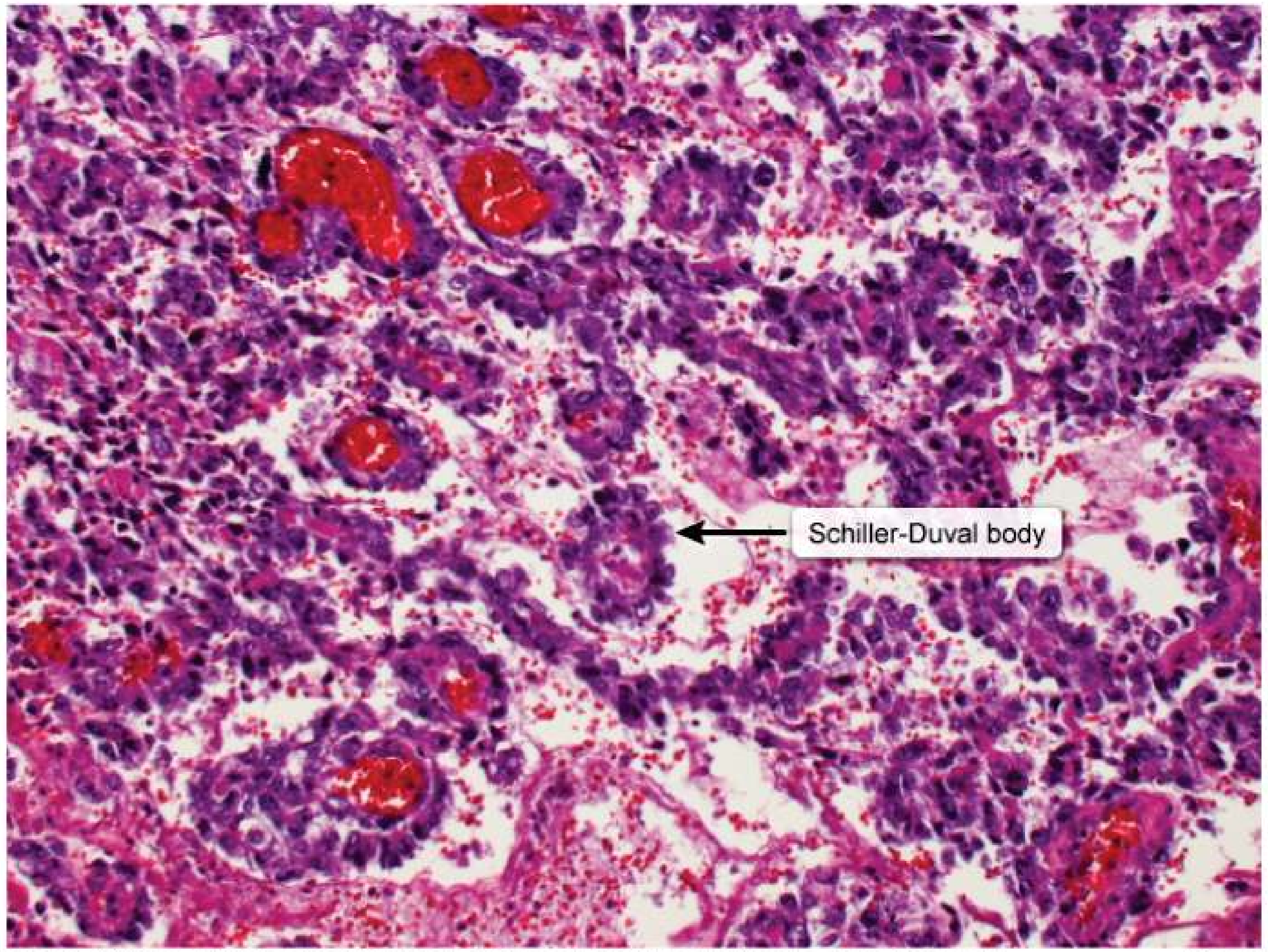
Endodermal sinus tumor



*Schiller Duval body: vessel surrounded by tumor cells creating a complex that resembles a glomerulus.

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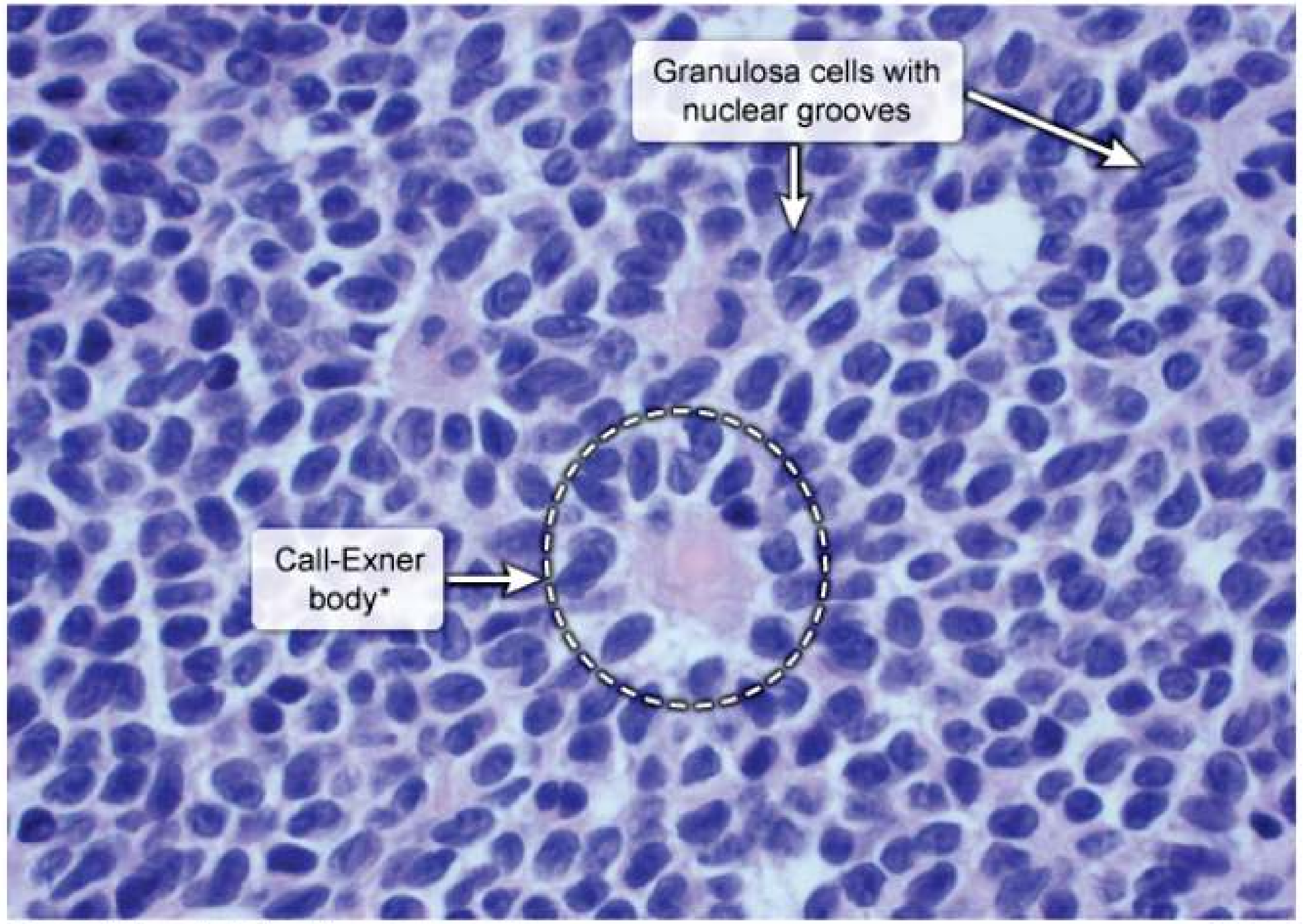
Granulosa cell tumor



*Eosinophilic material lined by granulosa cells

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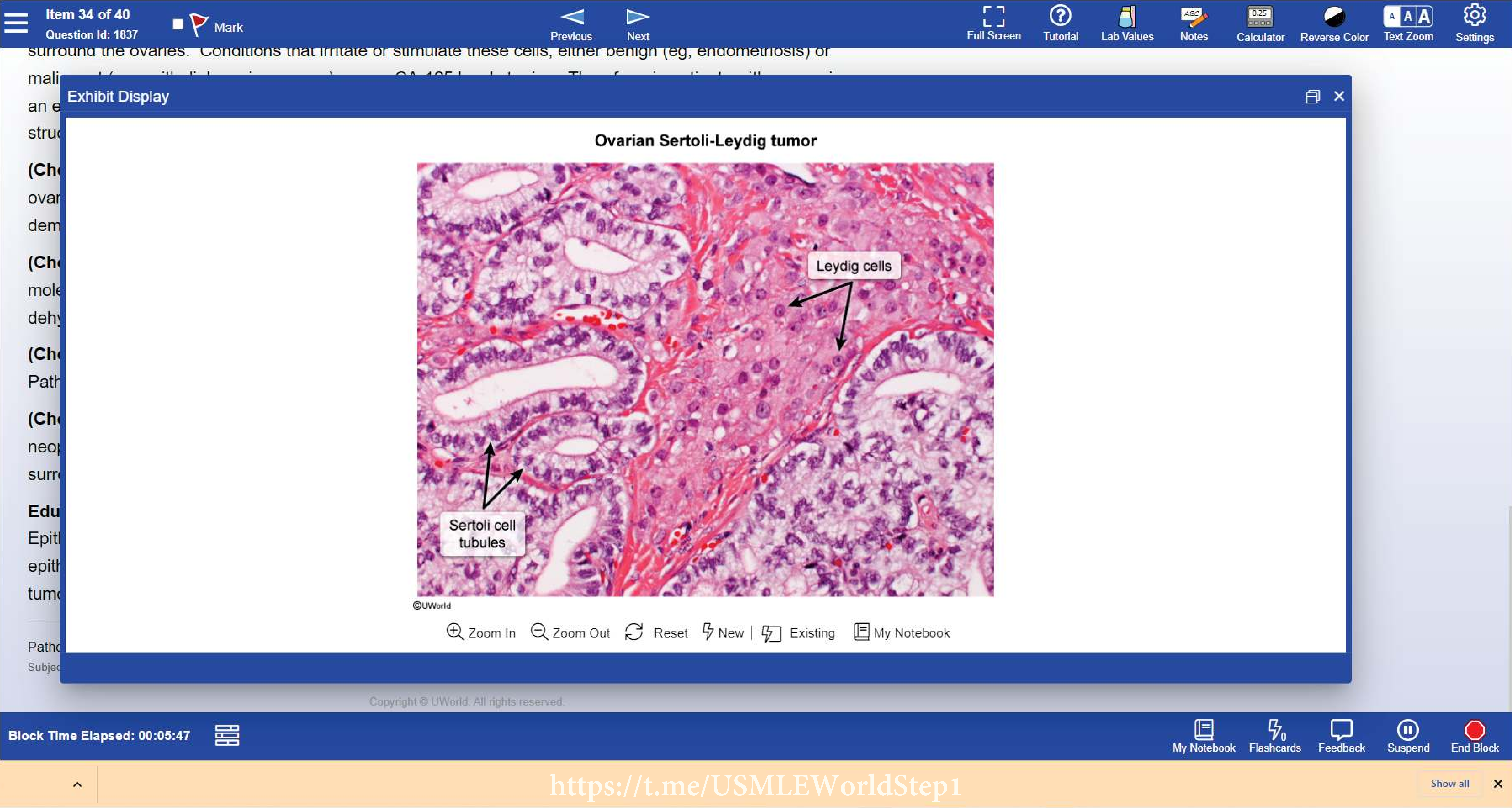

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Ovarian Sertoli-Leydig tumor

Leydig cells
Sertoli cell tubules

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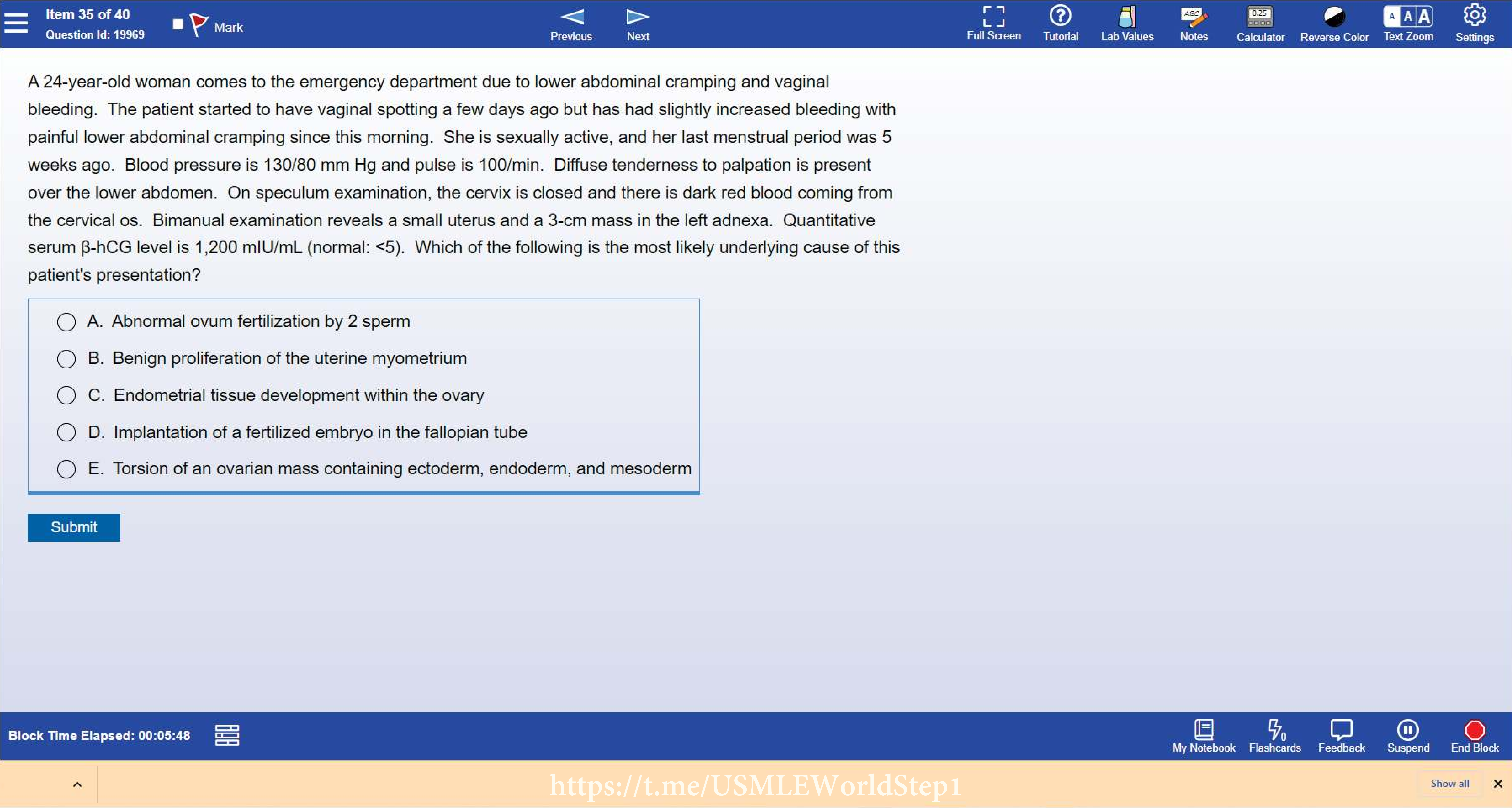
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A 24-year-old woman comes to the emergency department due to lower abdominal cramping and vaginal bleeding. The patient started to have vaginal spotting a few days ago but has had slightly increased bleeding with painful lower abdominal cramping since this morning. She is sexually active, and her last menstrual period was 5 weeks ago. Blood pressure is 130/80 mm Hg and pulse is 100/min. Diffuse tenderness to palpation is present over the lower abdomen. On speculum examination, the cervix is closed and there is dark red blood coming from the cervical os. Bimanual examination reveals a small uterus and a 3-cm mass in the left adnexa. Quantitative serum β-hCG level is 1,200 mIU/mL (normal: <5). Which of the following is the most likely underlying cause of this patient's presentation?

○ A. Abnormal ovum fertilization by 2 sperm
○ B. Benign proliferation of the uterine myometrium
○ C. Endometrial tissue development within the ovary
○ D. Implantation of a fertilized embryo in the fallopian tube
○ E. Torsion of an ovarian mass containing ectoderm, endoderm, and mesoderm

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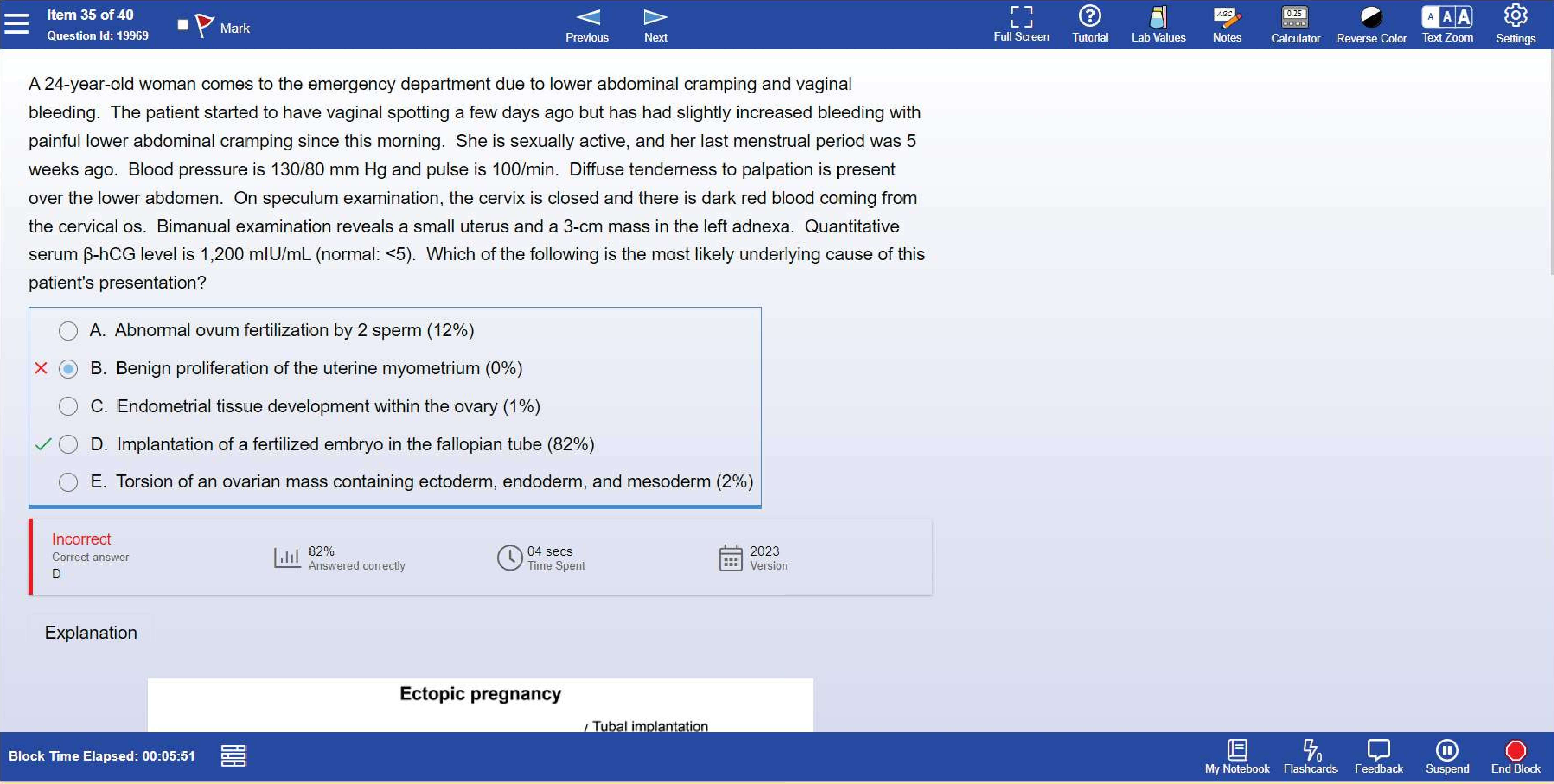
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○ A. Abnormal ovum fertilization by 2 sperm (12%)

✗ ● B. Benign proliferation of the uterine myometrium (0%)

○ C. Endometrial tissue development within the ovary (1%)

✓ ○ D. Implantation of a fertilized embryo in the fallopian tube (82%)

○ E. Torsion of an ovarian mass containing ectoderm, endoderm, and mesoderm (2%)

Incorrect
Correct answer
D

82%
Answered correctly

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Explanation

Ectopic pregnancy

Tubal implantation
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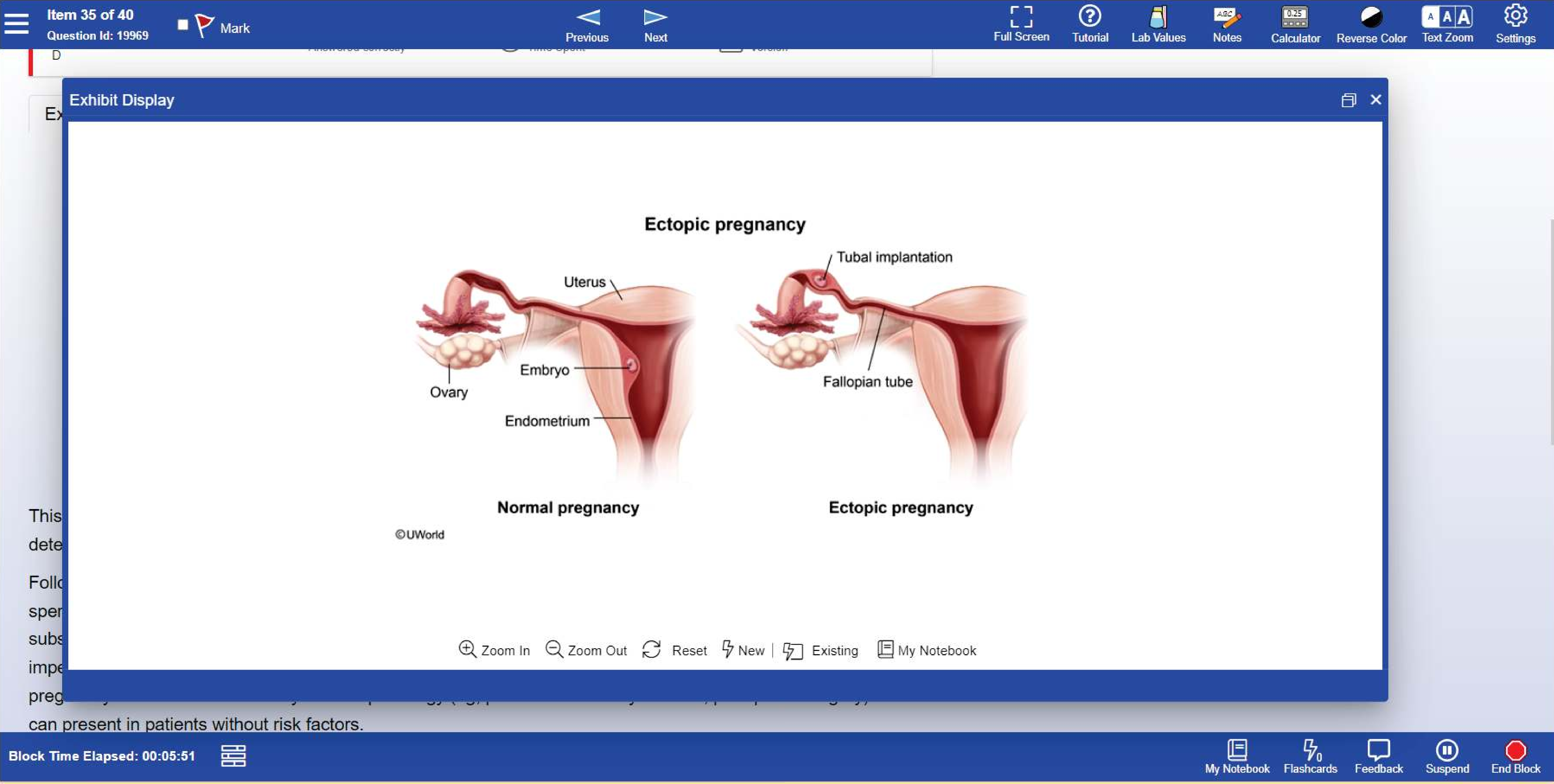
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Ectopic pregnancy
Tubal implantation
Uterus
Embryo
Ovary
Endometrium
Fallopian tube
Normal pregnancy
Ectopic pregnancy
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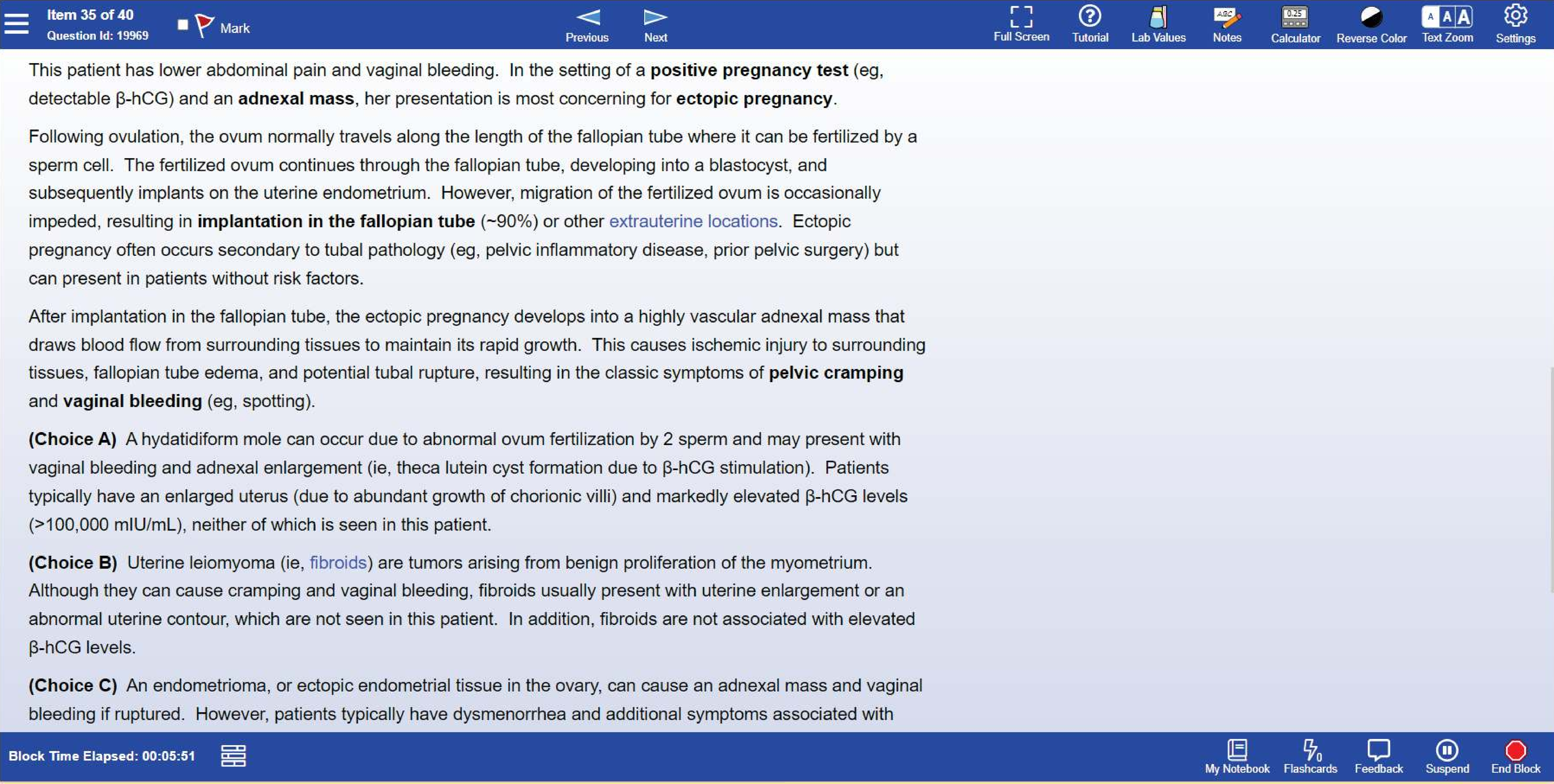

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This patient has lower abdominal pain and vaginal bleeding. In the setting of a **positive pregnancy test** (eg, detectable β-hCG) and an **adnexal mass**, her presentation is most concerning for **ectopic pregnancy**.

Following ovulation, the ovum normally travels along the length of the fallopian tube where it can be fertilized by a sperm cell. The fertilized ovum continues through the fallopian tube, developing into a blastocyst, and subsequently implants on the uterine endometrium. However, migration of the fertilized ovum is occasionally impeded, resulting in **implantation in the fallopian tube** (~90%) or other extrauterine locations. Ectopic pregnancy often occurs secondary to tubal pathology (eg, pelvic inflammatory disease, prior pelvic surgery) but can present in patients without risk factors.

After implantation in the fallopian tube, the ectopic pregnancy develops into a highly vascular adnexal mass that draws blood flow from surrounding tissues to maintain its rapid growth. This causes ischemic injury to surrounding tissues, fallopian tube edema, and potential tubal rupture, resulting in the classic symptoms of **pelvic cramping** and **vaginal bleeding** (eg, spotting).

(Choice A) A hydatidiform mole can occur due to abnormal ovum fertilization by 2 sperm and may present with vaginal bleeding and adnexal enlargement (ie, theca lutein cyst formation due to β-hCG stimulation). Patients typically have an enlarged uterus (due to abundant growth of chorionic villi) and markedly elevated β-hCG levels (>100,000 mIU/mL), neither of which is seen in this patient.

(Choice B) Uterine leiomyoma (ie, fibroids) are tumors arising from benign proliferation of the myometrium. Although they can cause cramping and vaginal bleeding, fibroids usually present with uterine enlargement or an abnormal uterine contour, which are not seen in this patient. In addition, fibroids are not associated with elevated β-hCG levels.

(Choice C) An endometrioma, or ectopic endometrial tissue in the ovary, can cause an adnexal mass and vaginal bleeding if ruptured. However, patients typically have dysmenorrhea and additional symptoms associated with

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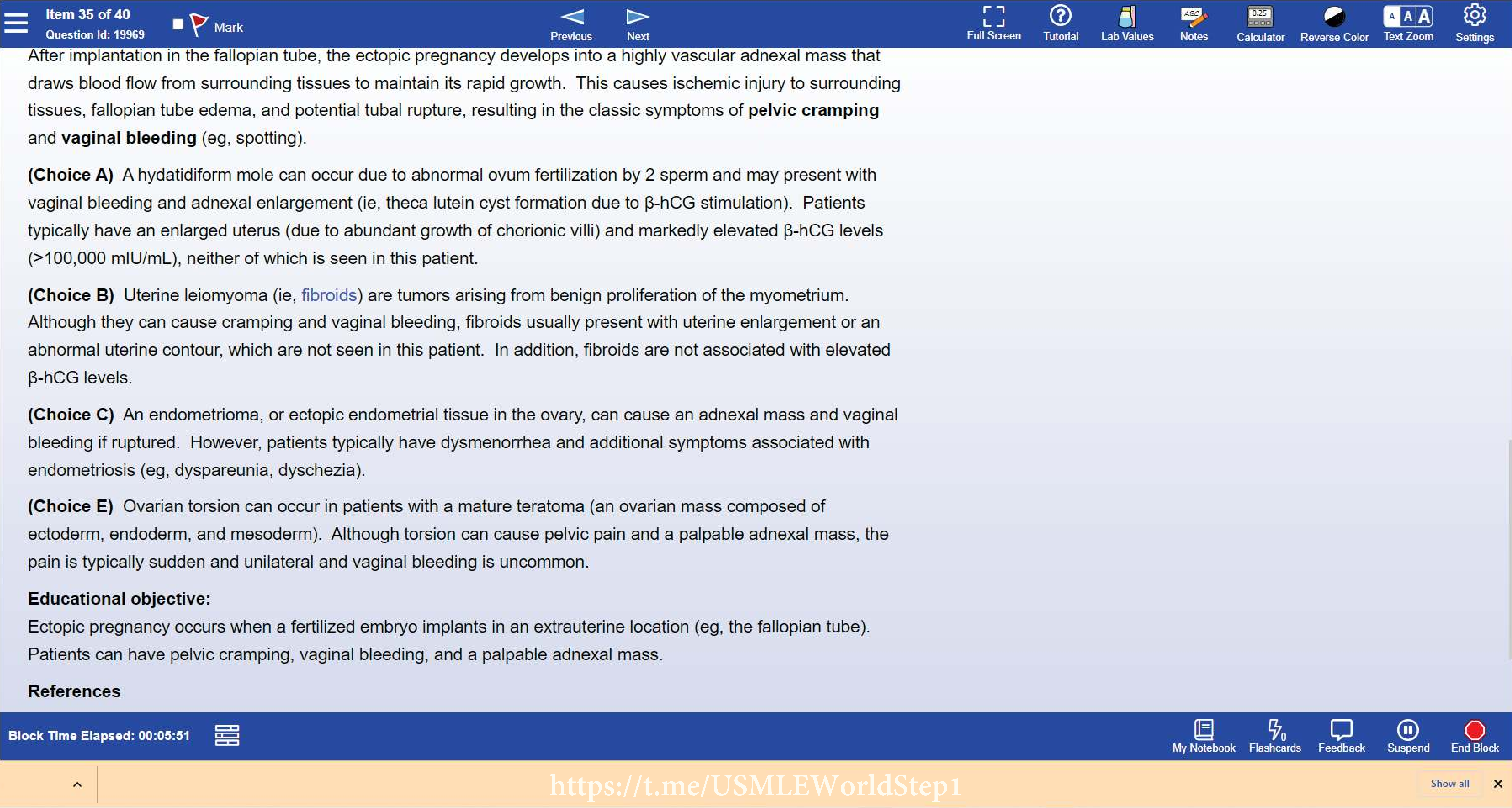
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(Choice C) An endometrioma, or ectopic endometrial tissue in the ovary, can cause an adnexal mass and vaginal bleeding if ruptured. However, patients typically have dysmenorrhea and additional symptoms associated with endometriosis (eg, dyspareunia, dyschezia).

(Choice E) Ovarian torsion can occur in patients with a mature teratoma (an ovarian mass composed of ectoderm, endoderm, and mesoderm). Although torsion can cause pelvic pain and a palpable adnexal mass, the pain is typically sudden and unilateral and vaginal bleeding is uncommon.

Educational objective:

Ectopic pregnancy occurs when a fertilized embryo implants in an extrauterine location (eg, the fallopian tube). Patients can have pelvic cramping, vaginal bleeding, and a palpable adnexal mass.

References

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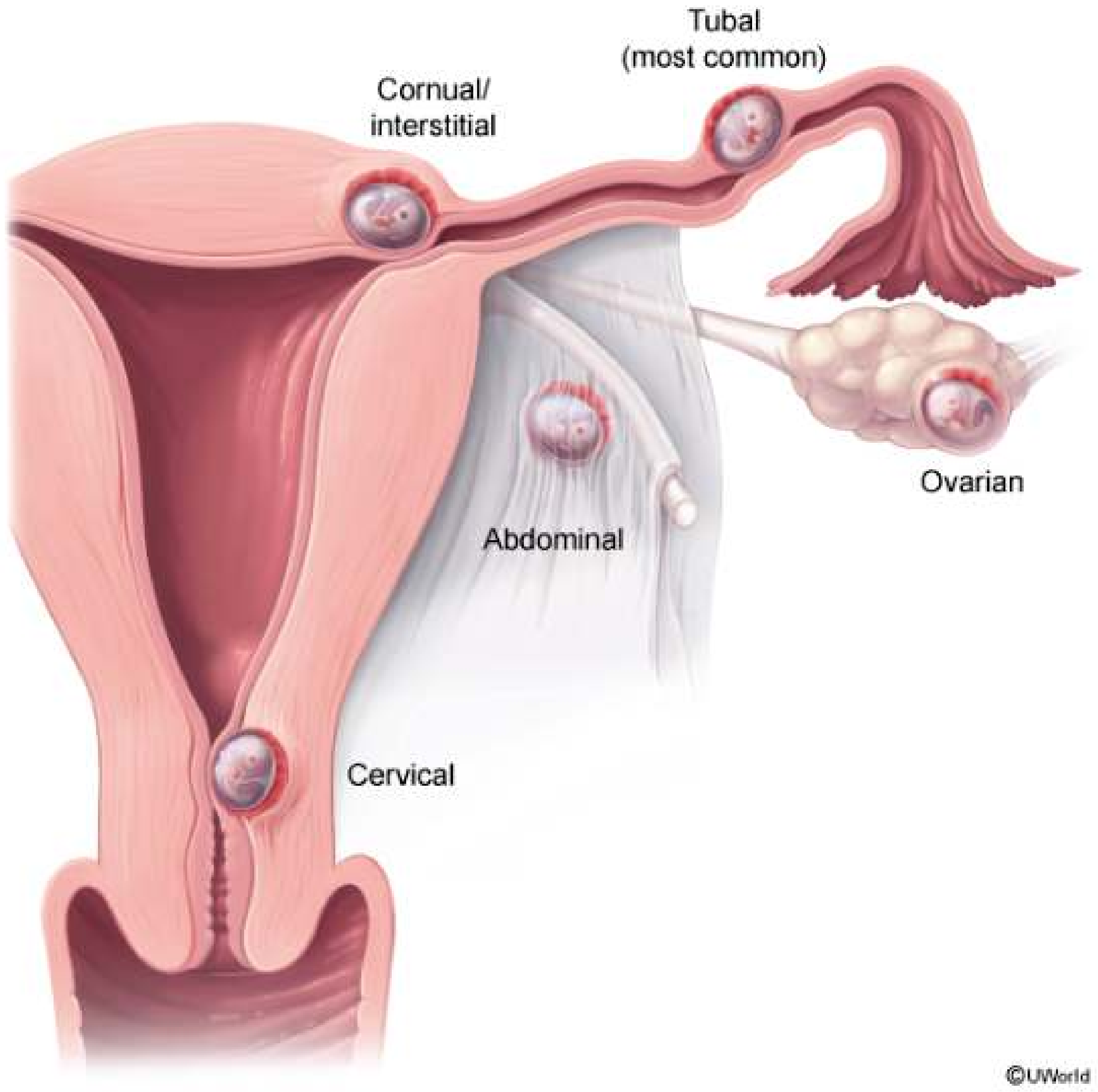
Ectopic pregnancy locations


Tubal
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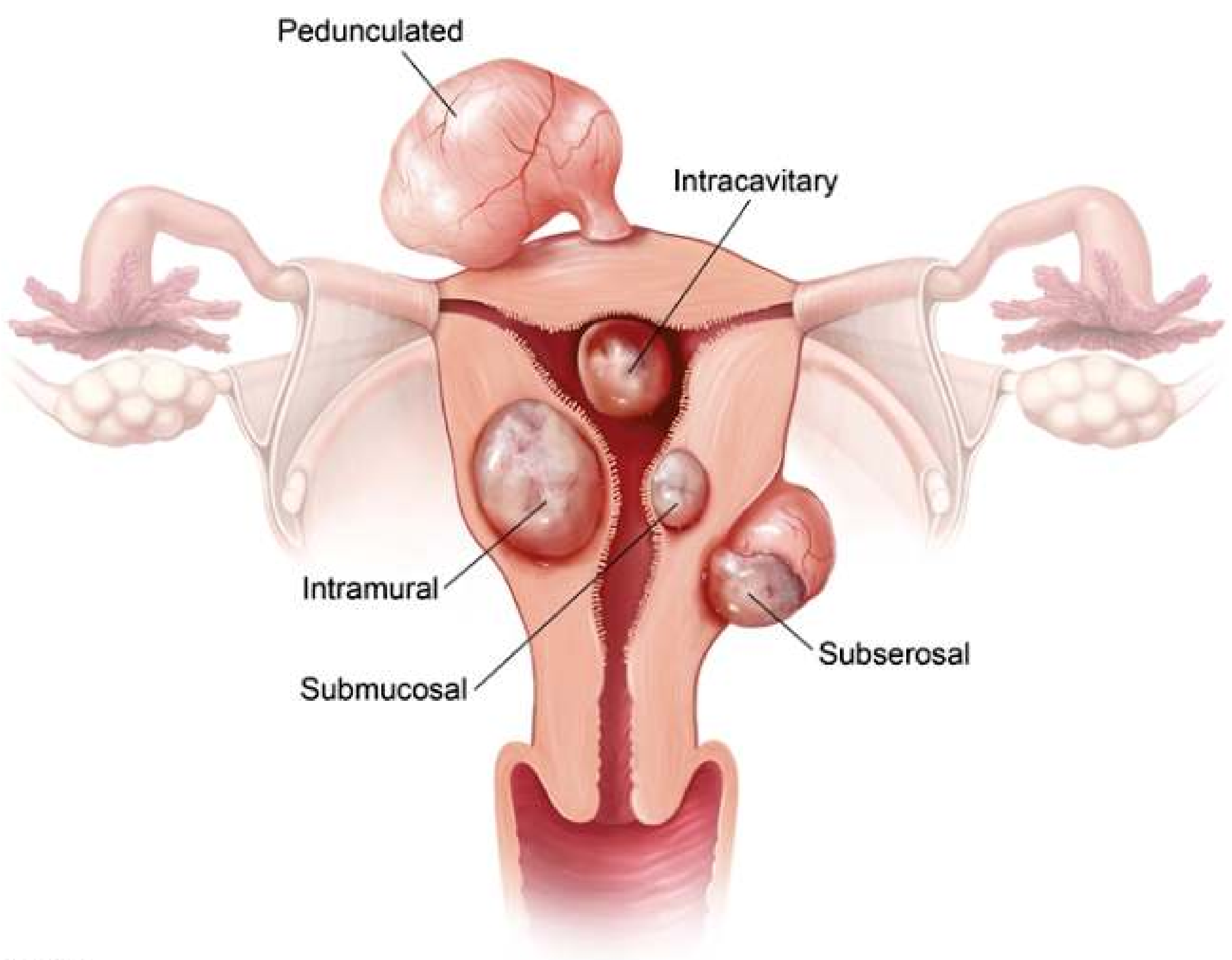
Uterine fibroids


Pedunculated
Intracavitary
Intramural
Subserosal
Submucosal

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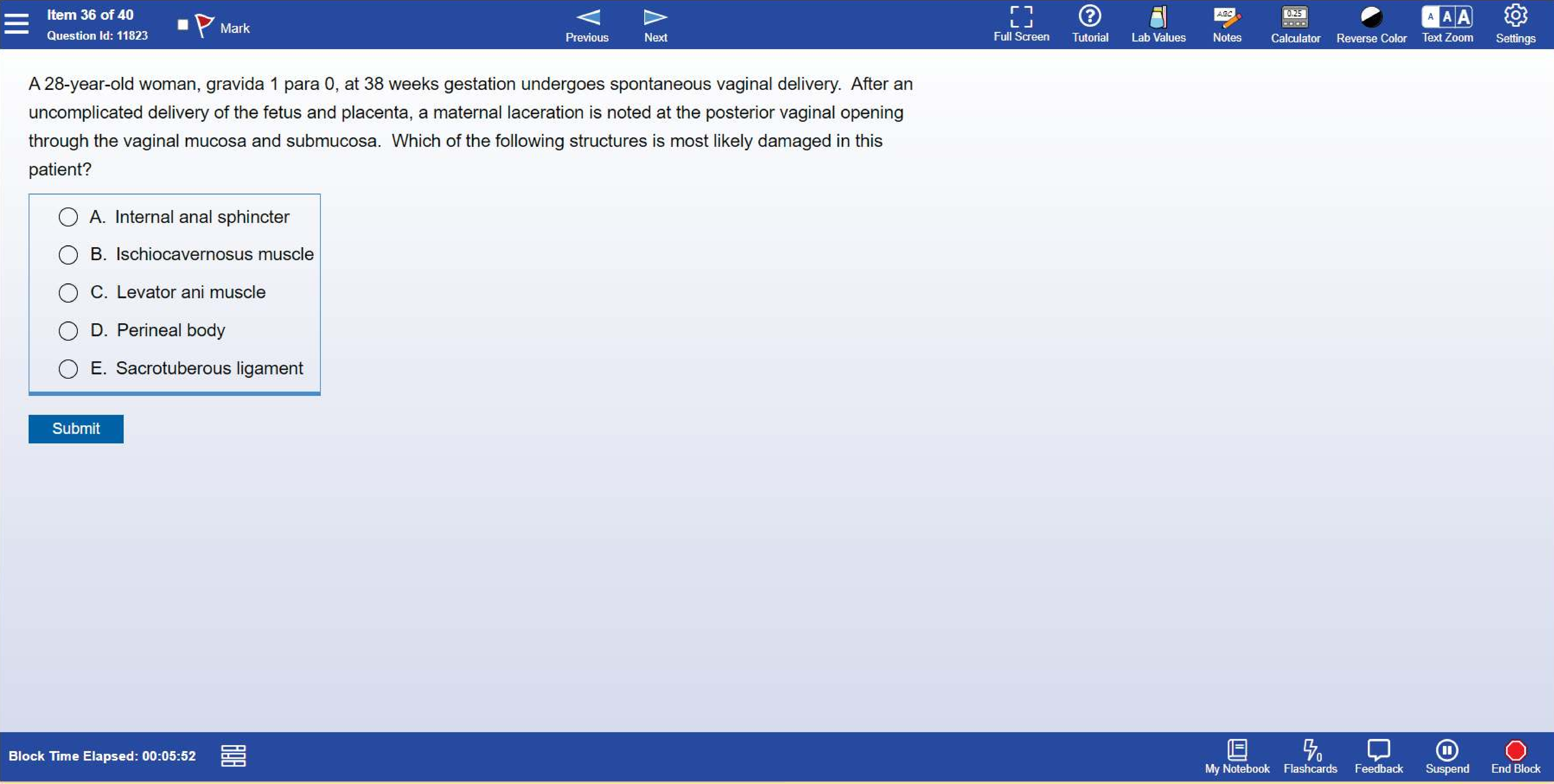

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A 28-year-old woman, gravida 1 para 0, at 38 weeks gestation undergoes spontaneous vaginal delivery. After an uncomplicated delivery of the fetus and placenta, a maternal laceration is noted at the posterior vaginal opening through the vaginal mucosa and submucosa. Which of the following structures is most likely damaged in this patient?

○ A. Internal anal sphincter
○ B. Ischiocavernosus muscle
○ C. Levator ani muscle
○ D. Perineal body
○ E. Sacrotuberous ligament

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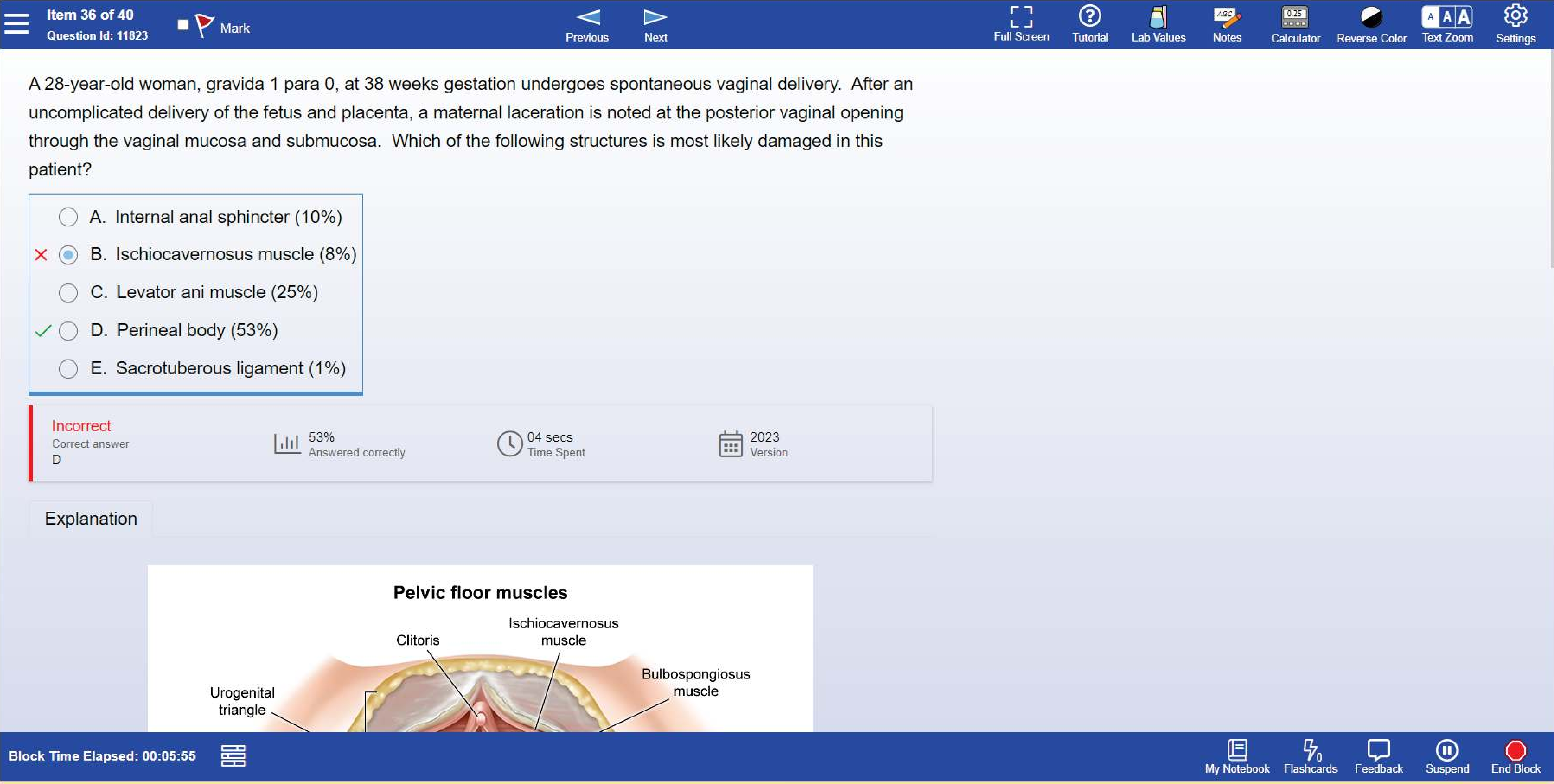
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A 28-year-old woman, gravida 1 para 0, at 38 weeks gestation undergoes spontaneous vaginal delivery. After an uncomplicated delivery of the fetus and placenta, a maternal laceration is noted at the posterior vaginal opening through the vaginal mucosa and submucosa. Which of the following structures is most likely damaged in this patient?

○ A. Internal anal sphincter (10%)
✗ ● B. Ischiocavernosus muscle (8%)
○ C. Levator ani muscle (25%)
✓ ○ D. Perineal body (53%)
○ E. Sacrotuberous ligament (1%)

Incorrect
Correct answer
D

53%
Answered correctly

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Explanation

Pelvic floor muscles

Clitoris
Ischiocavernosus muscle
Bulbospongiosus muscle
Urogenital triangle
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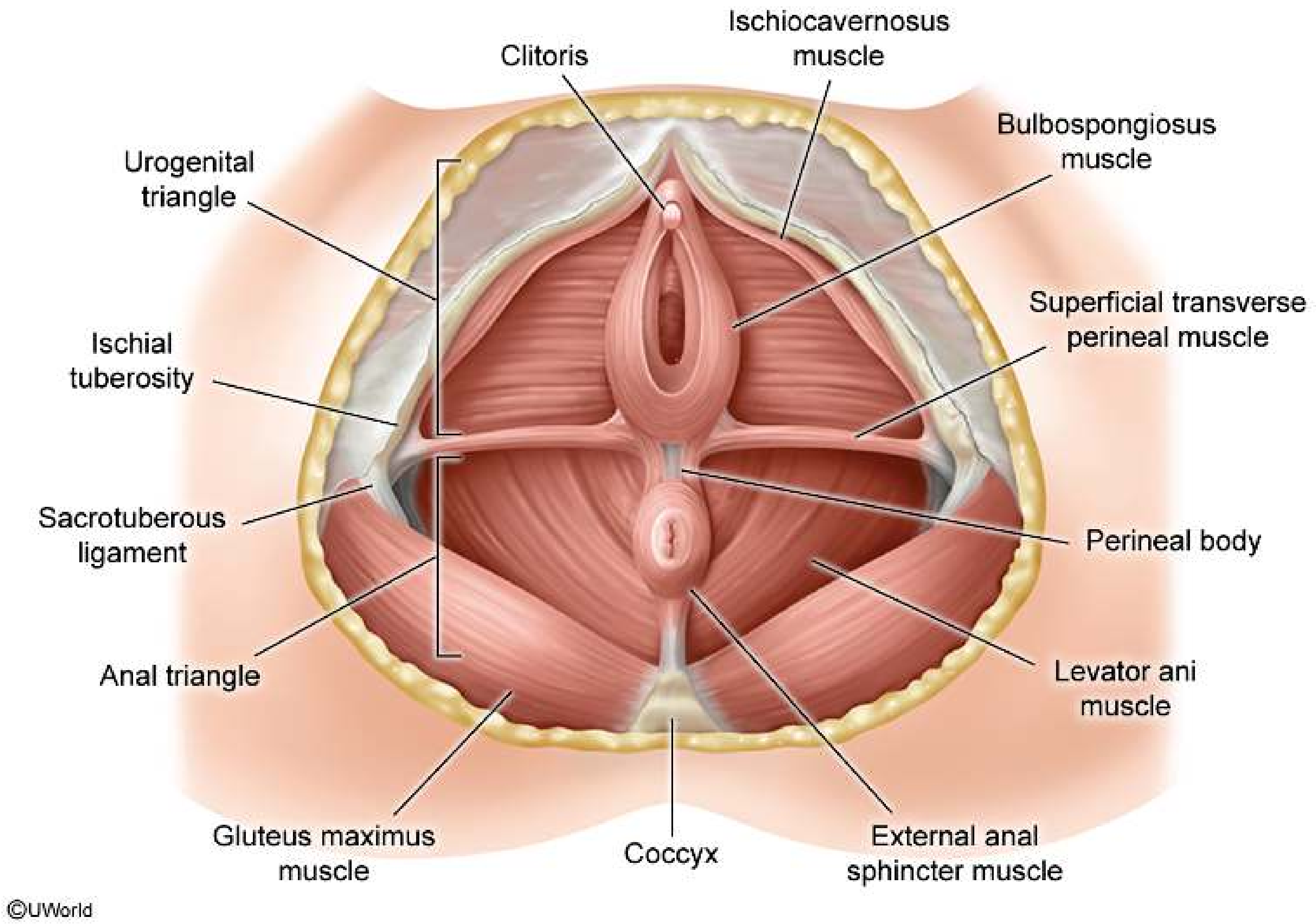
Pelvic floor muscles


Clitoris
Ischiocavernosus muscle
Bulbospongiosus muscle
Urogenital triangle
Superficial transverse perineal muscle
Ischial tuberosity
Sacrotuberous ligament
Perineal body
Levator ani muscle
Anal triangle
Gluteus maximus muscle
Coccyx
External anal sphincter muscle
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fascial, and fibrous components. The structures forming and attaching to the perineal body include the:

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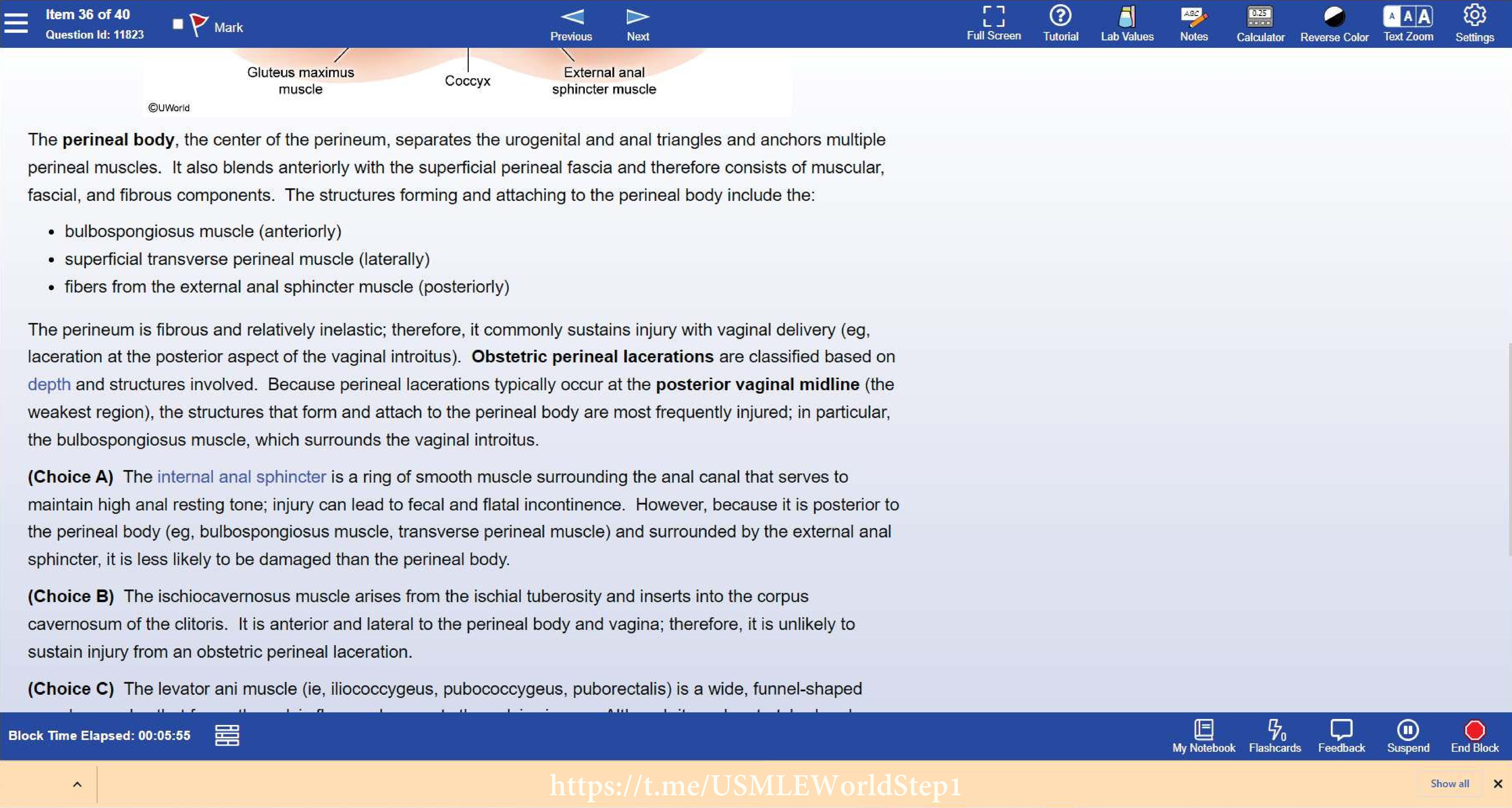
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Coccyx
External anal sphincter muscle
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The **perineal body**, the center of the perineum, separates the urogenital and anal triangles and anchors multiple perineal muscles. It also blends anteriorly with the superficial perineal fascia and therefore consists of muscular, fascial, and fibrous components. The structures forming and attaching to the perineal body include the:

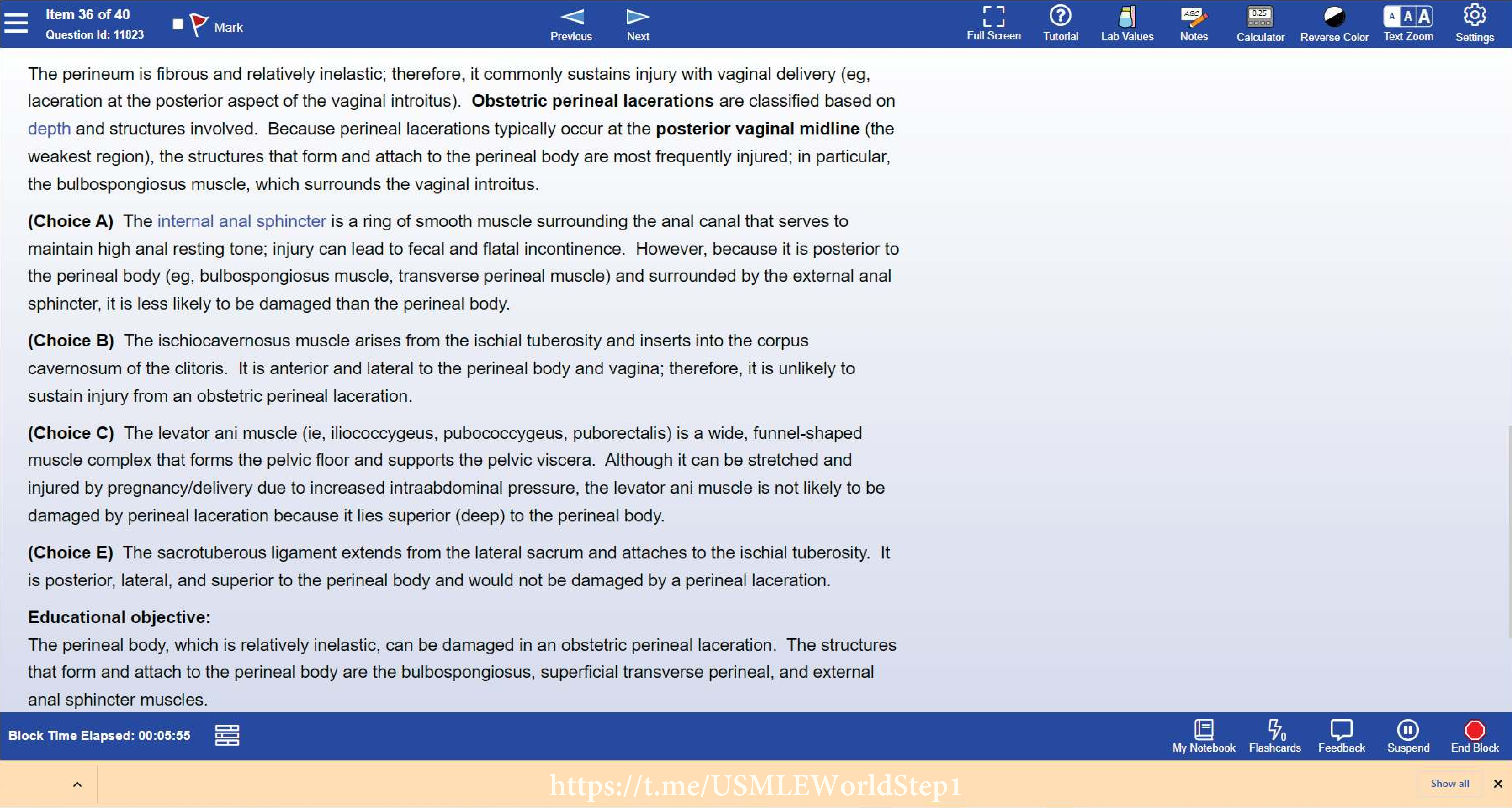
- bulbospongiosus muscle (anteriorly)
- superficial transverse perineal muscle (laterally)
- fibers from the external anal sphincter muscle (posteriorly)

The perineum is fibrous and relatively inelastic; therefore, it commonly sustains injury with vaginal delivery (eg, laceration at the posterior aspect of the vaginal introitus). **Obstetric perineal lacerations** are classified based on depth and structures involved. Because perineal lacerations typically occur at the **posterior vaginal midline** (the weakest region), the structures that form and attach to the perineal body are most frequently injured; in particular, the bulbospongiosus muscle, which surrounds the vaginal introitus.

(Choice A) The internal anal sphincter is a ring of smooth muscle surrounding the anal canal that serves to maintain high anal resting tone; injury can lead to fecal and flatal incontinence. However, because it is posterior to the perineal body (eg, bulbospongiosus muscle, transverse perineal muscle) and surrounded by the external anal sphincter, it is less likely to be damaged than the perineal body.

(Choice B) The ischiocavernosus muscle arises from the ischial tuberosity and inserts into the corpus cavernosum of the clitoris. It is anterior and lateral to the perineal body and vagina; therefore, it is unlikely to sustain injury from an obstetric perineal laceration.

(Choice C) The levator ani muscle (ie, iliococcygeus, pubococcygeus, puborectalis) is a wide, funnel-shaped



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(Choice C) The levator ani muscle (ie, iliococcygeus, pubococcygeus, puborectalis) is a wide, funnel-shaped muscle complex that forms the pelvic floor and supports the pelvic viscera. Although it can be stretched and injured by pregnancy/delivery due to increased intraabdominal pressure, the levator ani muscle is not likely to be damaged by perineal laceration because it lies superior (deep) to the perineal body.

(Choice E) The sacrotuberous ligament extends from the lateral sacrum and attaches to the ischial tuberosity. It is posterior, lateral, and superior to the perineal body and would not be damaged by a perineal laceration.

Educational objective:
The perineal body, which is relatively inelastic, can be damaged in an obstetric perineal laceration. The structures that form and attach to the perineal body are the bulbospongiosus, superficial transverse perineal, and external anal sphincter muscles.

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External anal

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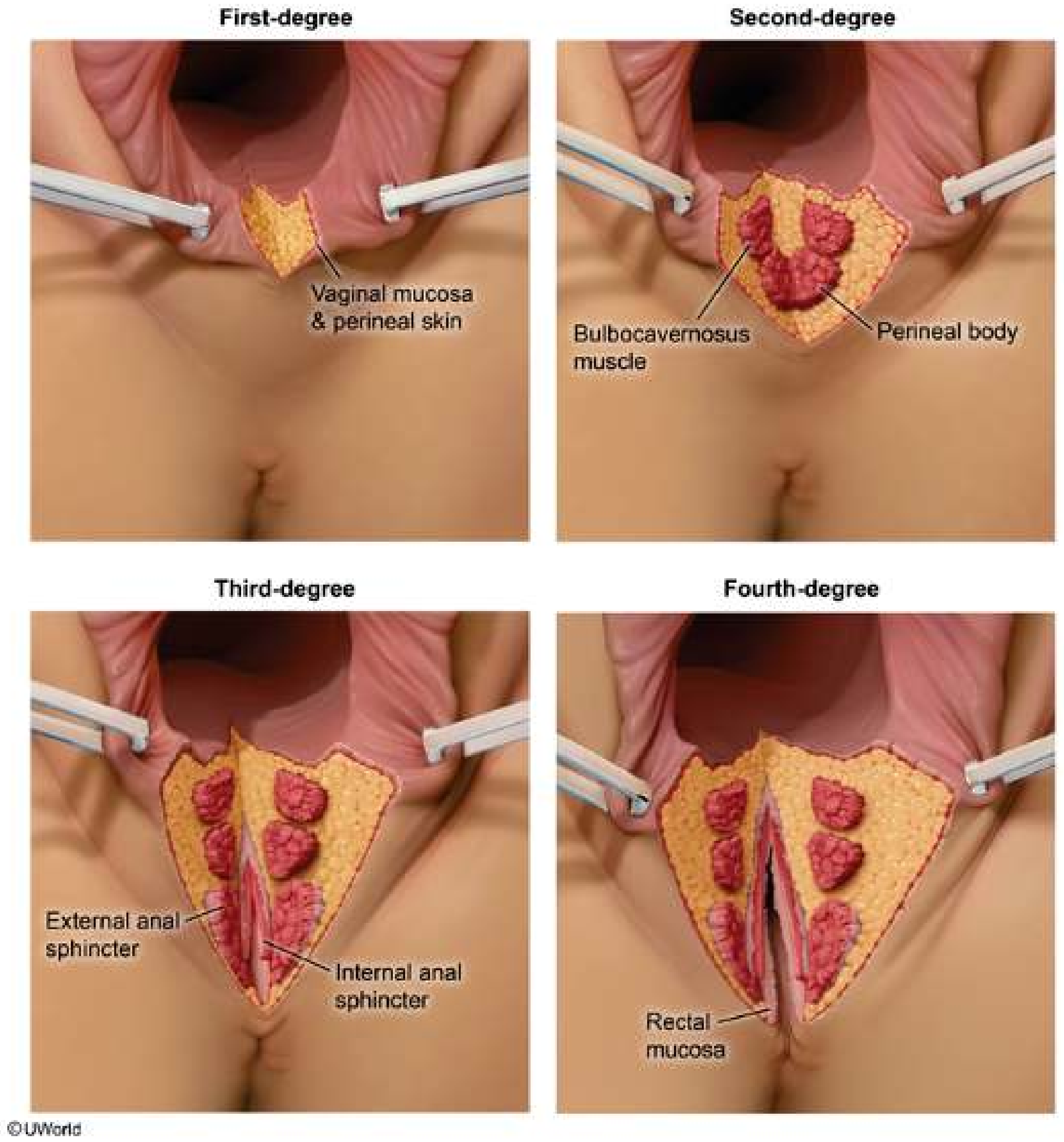
Perineal lacerations



First-degree
Vaginal mucosa & perineal skin
Second-degree
Bulbocavernosus muscle
Perineal body
Third-degree
External anal sphincter
Internal anal sphincter
Fourth-degree
Rectal mucosa
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(Choice C) The levator ani muscle (ie, iliococcygeus, pubococcygeus, puborectalis) is a wide, funnel-shaped muscle complex that forms the pelvic floor and supports the pelvic viscera. Although it can be stretched and

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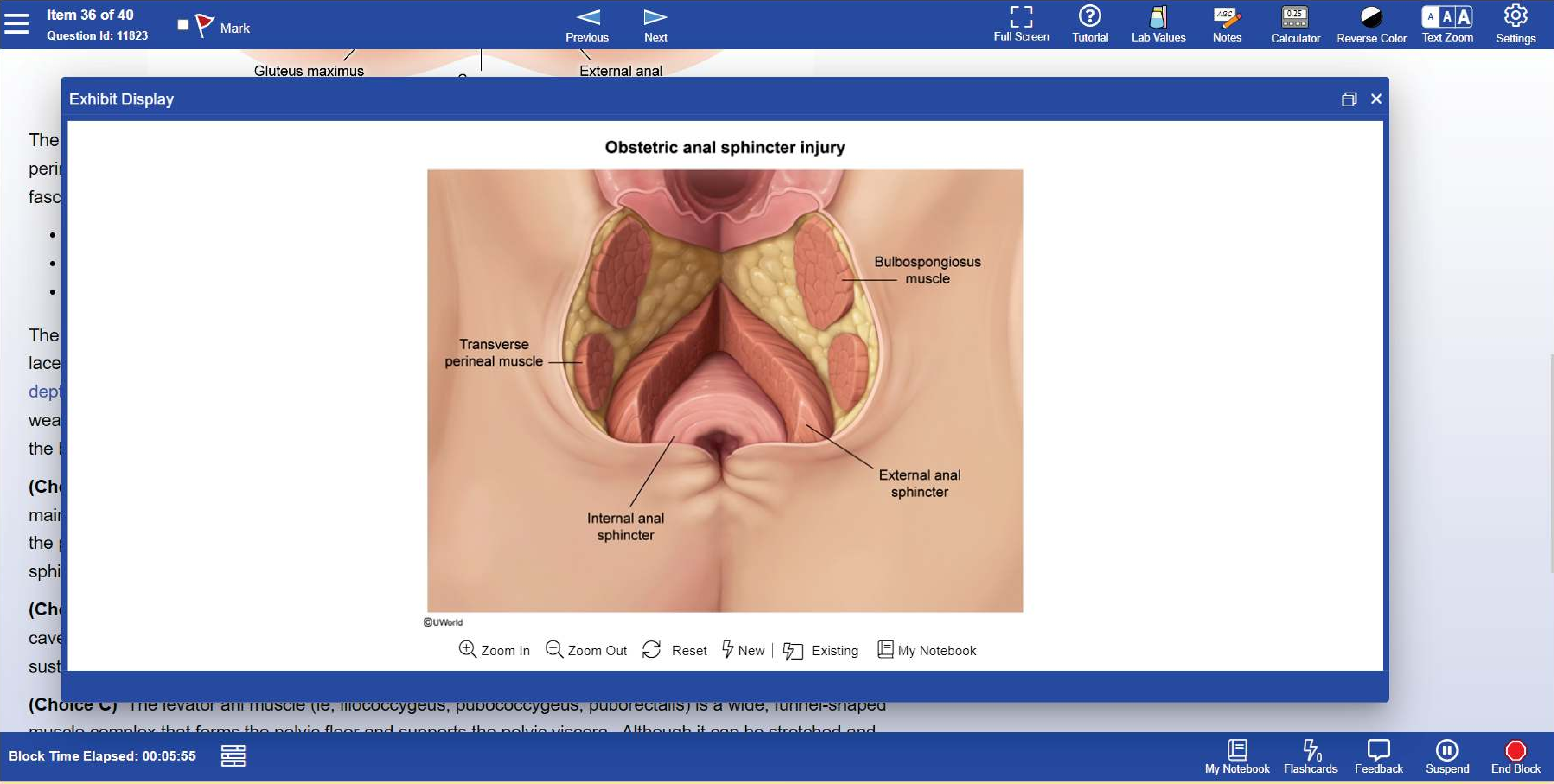
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Gluteus maximus
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Bulbospongiosus muscle
Transverse perineal muscle
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Obstetric anal sphincter injury

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(Choice C) The levator ani muscle (ie, iliococcygeus, pubococcygeus, puborectalis) is a wide, funnel-shaped muscle complex that forms the pelvic floor and supports the pelvic viscera. Although it can be stretched and

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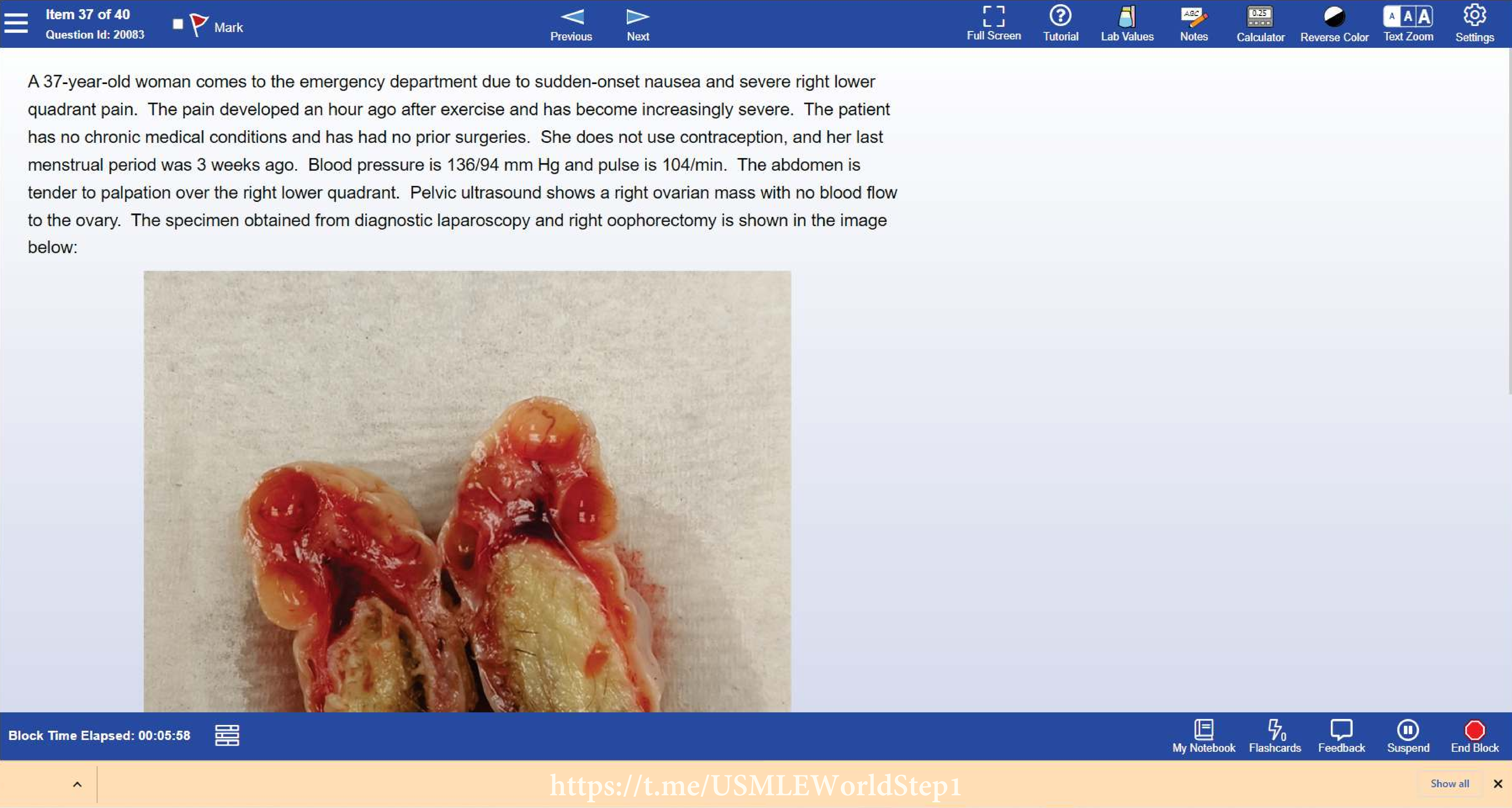
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A 37-year-old woman comes to the emergency department due to sudden-onset nausea and severe right lower quadrant pain. The pain developed an hour ago after exercise and has become increasingly severe. The patient has no chronic medical conditions and has had no prior surgeries. She does not use contraception, and her last menstrual period was 3 weeks ago. Blood pressure is 136/94 mm Hg and pulse is 104/min. The abdomen is tender to palpation over the right lower quadrant. Pelvic ultrasound shows a right ovarian mass with no blood flow to the ovary. The specimen obtained from diagnostic laparoscopy and right oophorectomy is shown in the image below:

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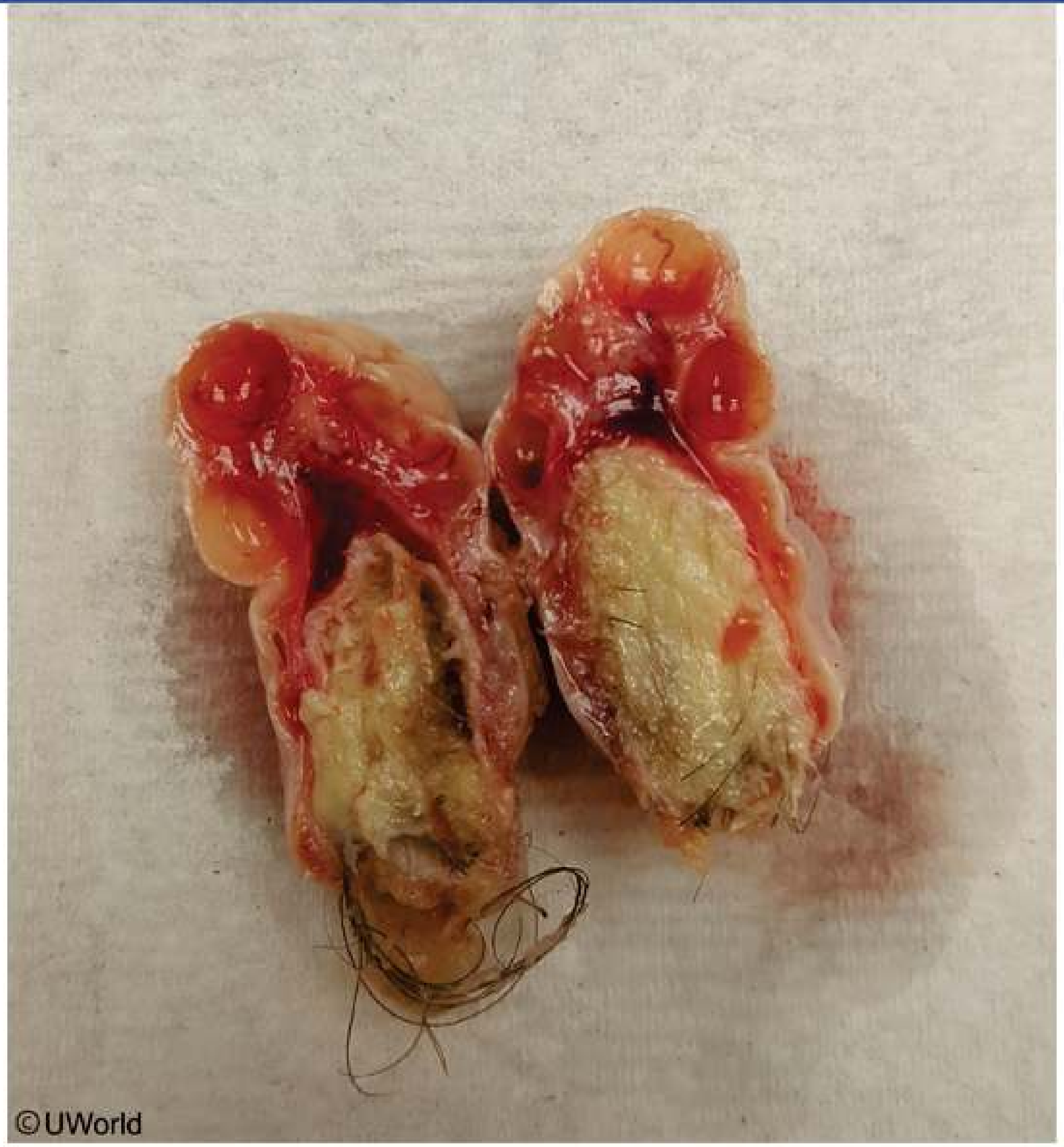
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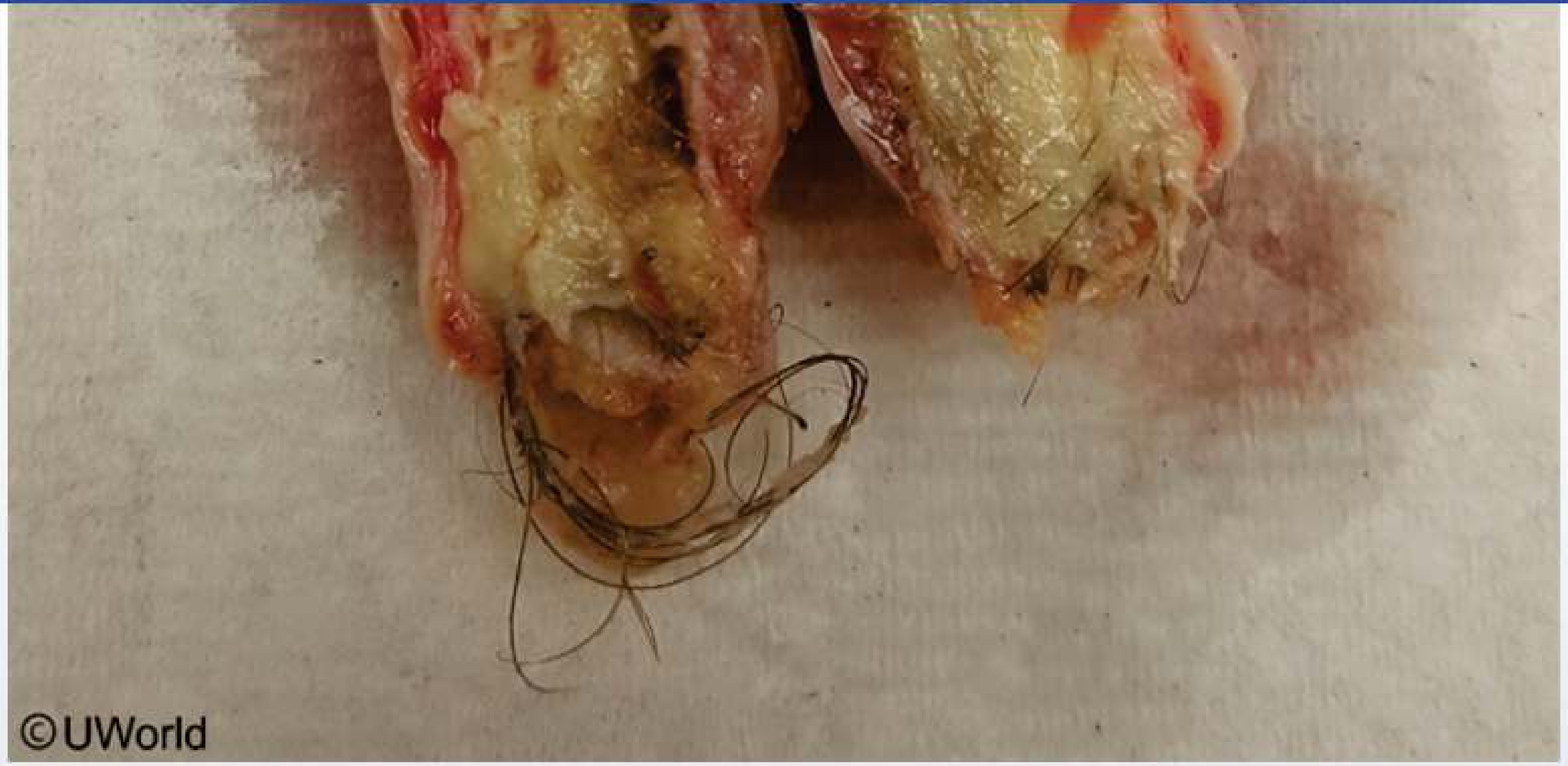

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Which of the following is the most likely diagnosis?

- ○ A. Ectopic pregnancy
- ○ B. Endometrioma
- ○ C. Mature cystic teratoma
- ○ D. Mucinous cystadenoma
- ○ E. Ovarian fibroma
- ○ F. Yolk sac tumor

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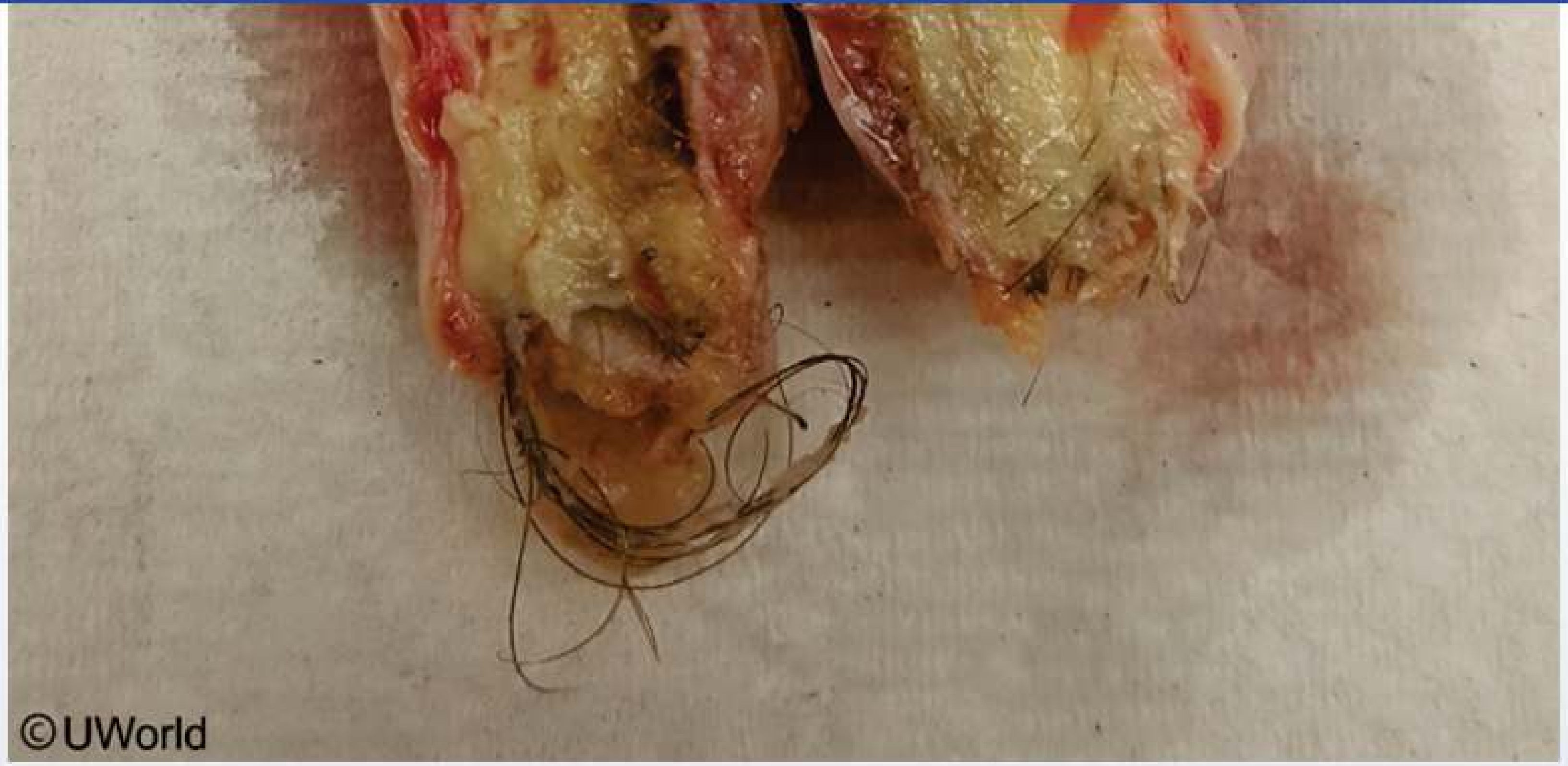

Which of the following is the most likely diagnosis?

- ○ A. Ectopic pregnancy (0%)
- ○ B. Endometrioma (0%)
- ✓ ● C. Mature cystic teratoma (96%)
- ○ D. Mucinous cystadenoma (0%)
- ○ E. Ovarian fibroma (0%)
- ○ F. Yolk sac tumor (1%)

Correct

96%
Answered correctly

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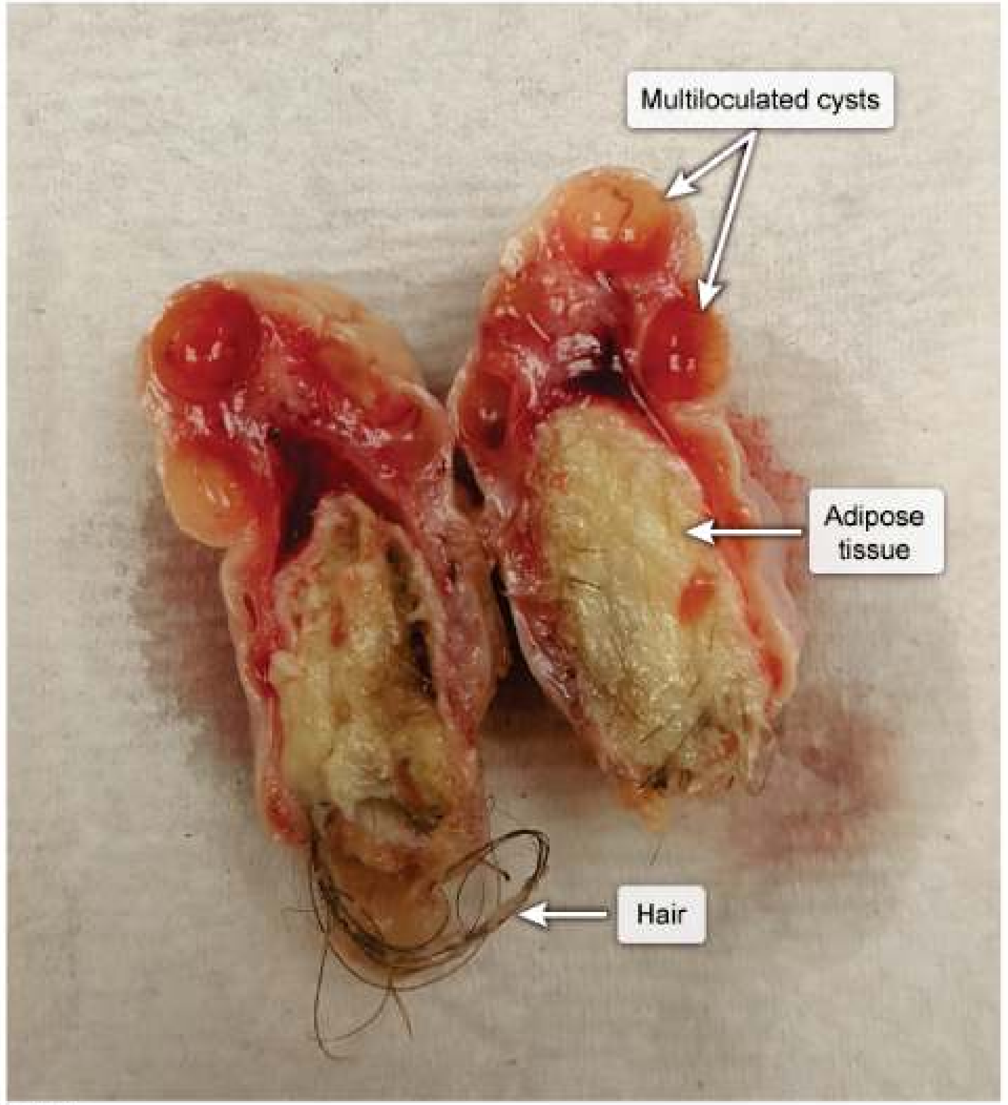
Mature cystic teratoma



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This patient with sudden, severe right lower quadrant pain and absent blood flow to the ovary has ovarian torsion

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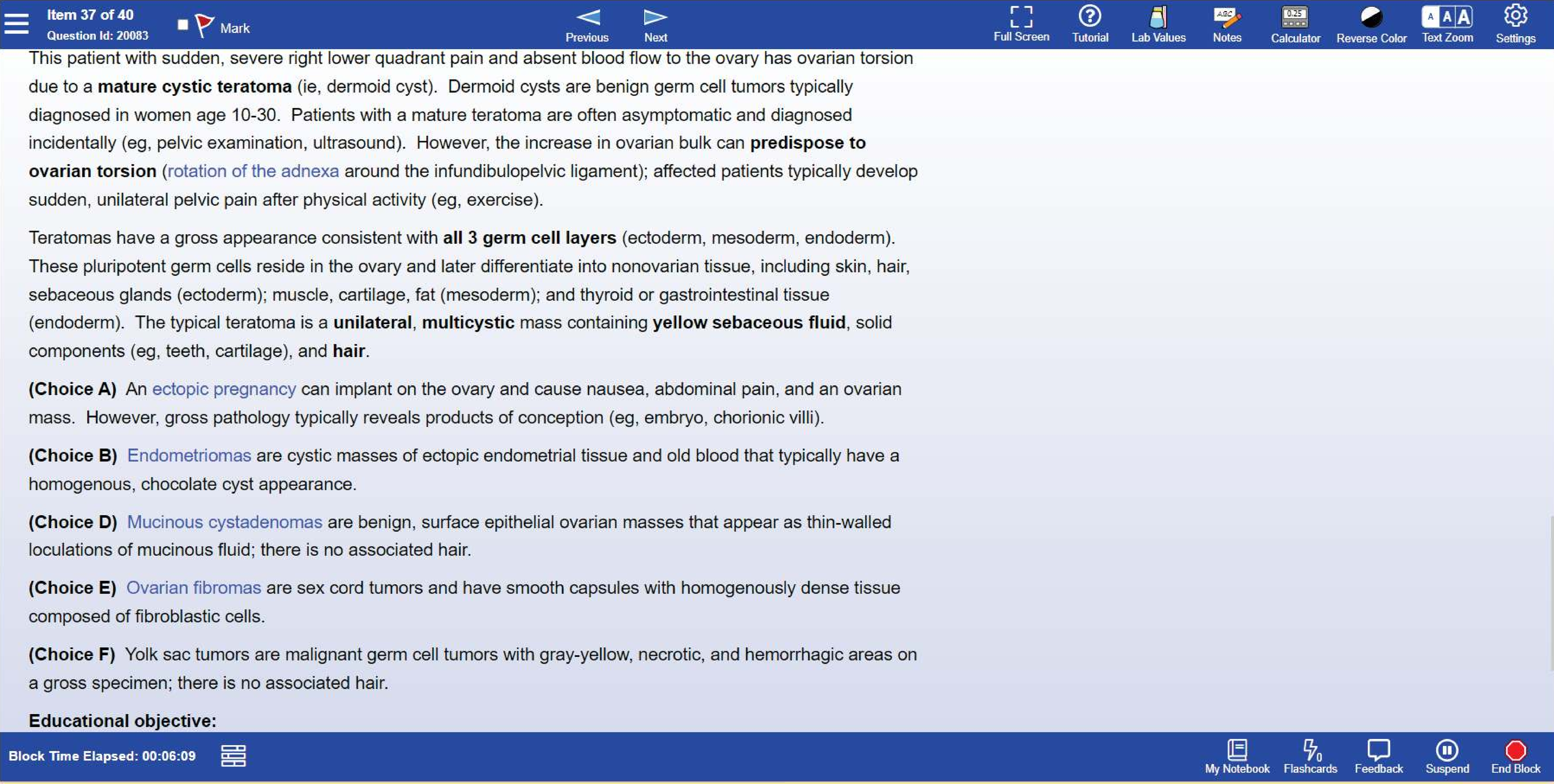
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This patient with sudden, severe right lower quadrant pain and absent blood flow to the ovary has ovarian torsion due to a **mature cystic teratoma** (ie, dermoid cyst). Dermoid cysts are benign germ cell tumors typically diagnosed in women age 10-30. Patients with a mature teratoma are often asymptomatic and diagnosed incidentally (eg, pelvic examination, ultrasound). However, the increase in ovarian bulk can **predispose to ovarian torsion** (rotation of the adnexa around the infundibulopelvic ligament); affected patients typically develop sudden, unilateral pelvic pain after physical activity (eg, exercise).

Teratomas have a gross appearance consistent with **all 3 germ cell layers** (ectoderm, mesoderm, endoderm). These pluripotent germ cells reside in the ovary and later differentiate into nonovarian tissue, including skin, hair, sebaceous glands (ectoderm); muscle, cartilage, fat (mesoderm); and thyroid or gastrointestinal tissue (endoderm). The typical teratoma is a **unilateral**, **multicystic** mass containing **yellow sebaceous fluid**, solid components (eg, teeth, cartilage), and **hair**.

(Choice A) An ectopic pregnancy can implant on the ovary and cause nausea, abdominal pain, and an ovarian mass. However, gross pathology typically reveals products of conception (eg, embryo, chorionic villi).

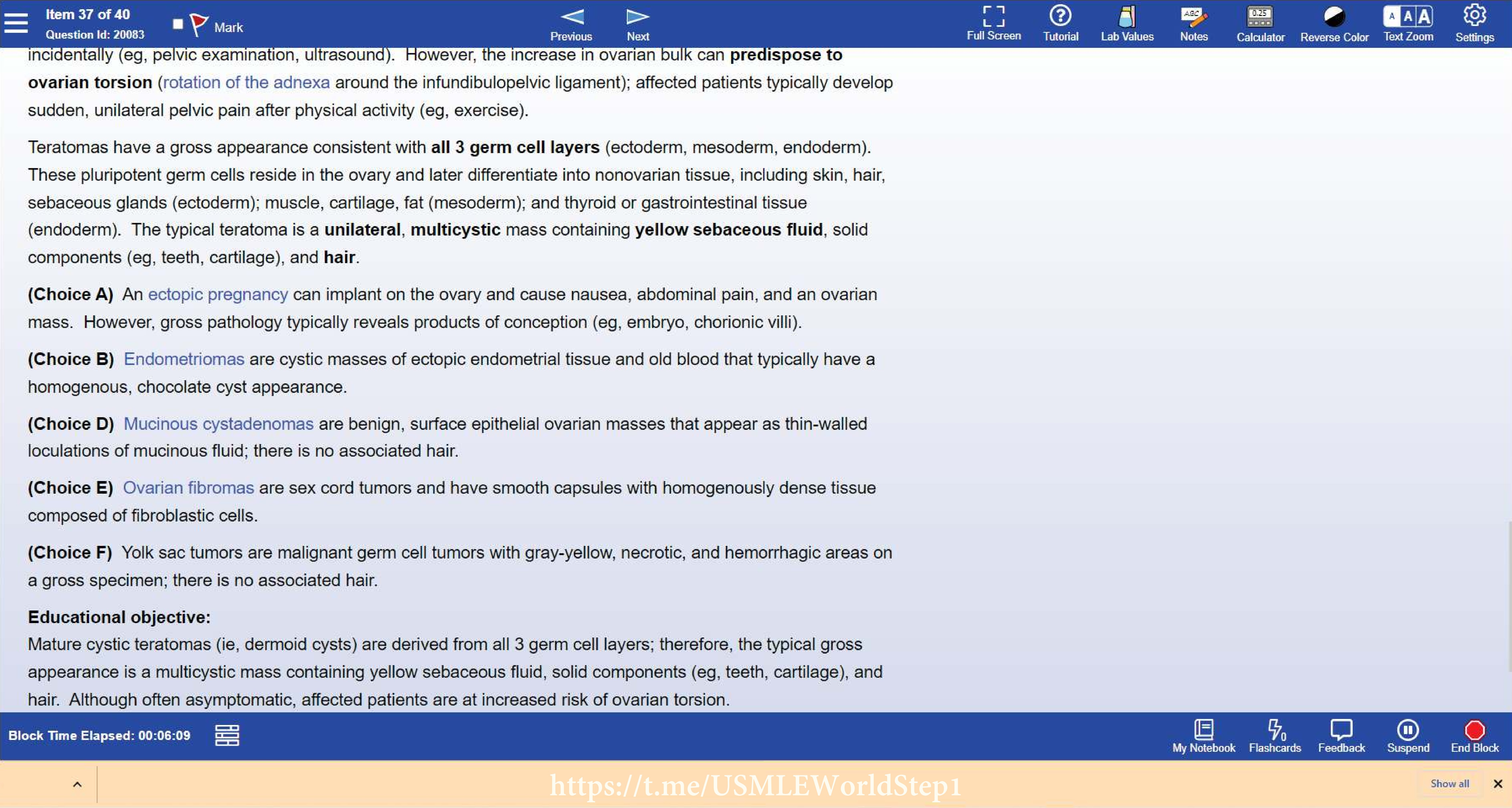
(Choice B) Endometriomas are cystic masses of ectopic endometrial tissue and old blood that typically have a homogenous, chocolate cyst appearance.

(Choice D) Mucinous cystadenomas are benign, surface epithelial ovarian masses that appear as thin-walled loculations of mucinous fluid; there is no associated hair.

(Choice E) Ovarian fibromas are sex cord tumors and have smooth capsules with homogenously dense tissue composed of fibroblastic cells.

(Choice F) Yolk sac tumors are malignant germ cell tumors with gray-yellow, necrotic, and hemorrhagic areas on a gross specimen; there is no associated hair.

Educational objective: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(Choice D) Mucinous cystadenomas are benign, surface epithelial ovarian masses that appear as thin-walled loculations of mucinous fluid; there is no associated hair.

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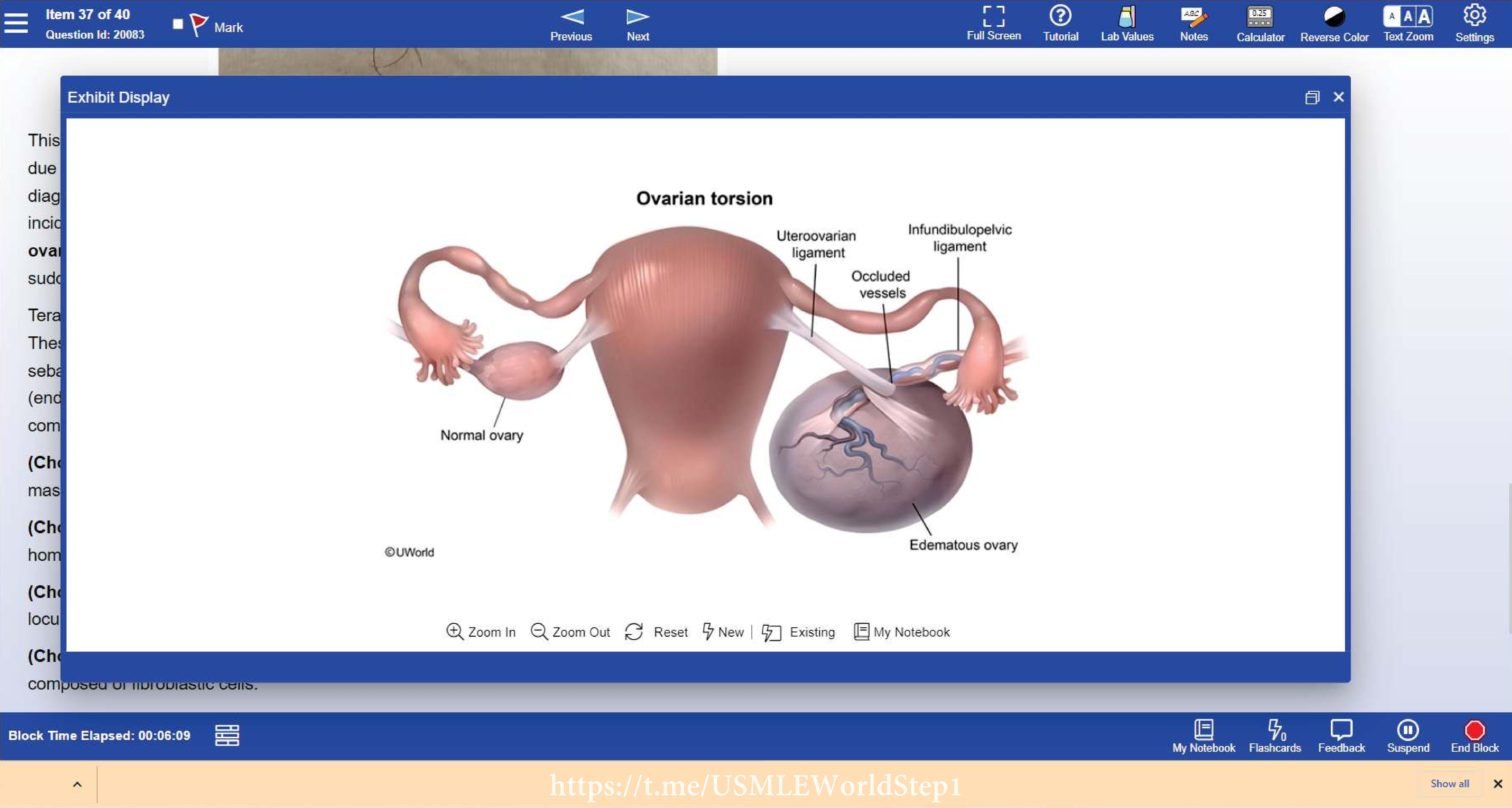
(Choice F) Yolk sac tumors are malignant germ cell tumors with gray-yellow, necrotic, and hemorrhagic areas on a gross specimen; there is no associated hair.

Educational objective:
Mature cystic teratomas (ie, dermoid cysts) are derived from all 3 germ cell layers; therefore, the typical gross appearance is a multicystic mass containing yellow sebaceous fluid, solid components (eg, teeth, cartilage), and hair. Although often asymptomatic, affected patients are at increased risk of ovarian torsion.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Ovarian torsion
Uteroovarian ligament
Infundibulopelvic ligament
Occluded vessels
Normal ovary
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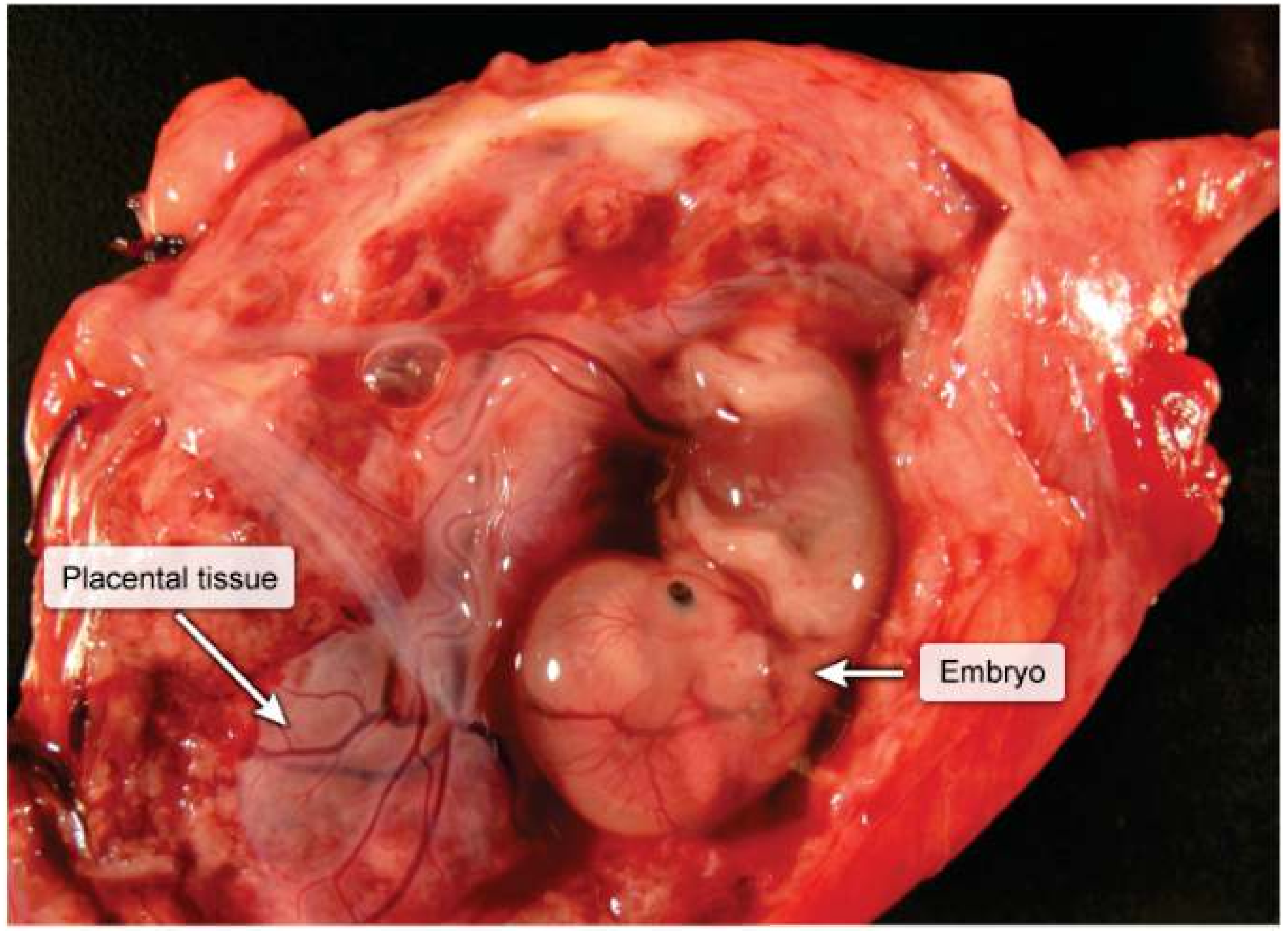
Ectopic pregnancy



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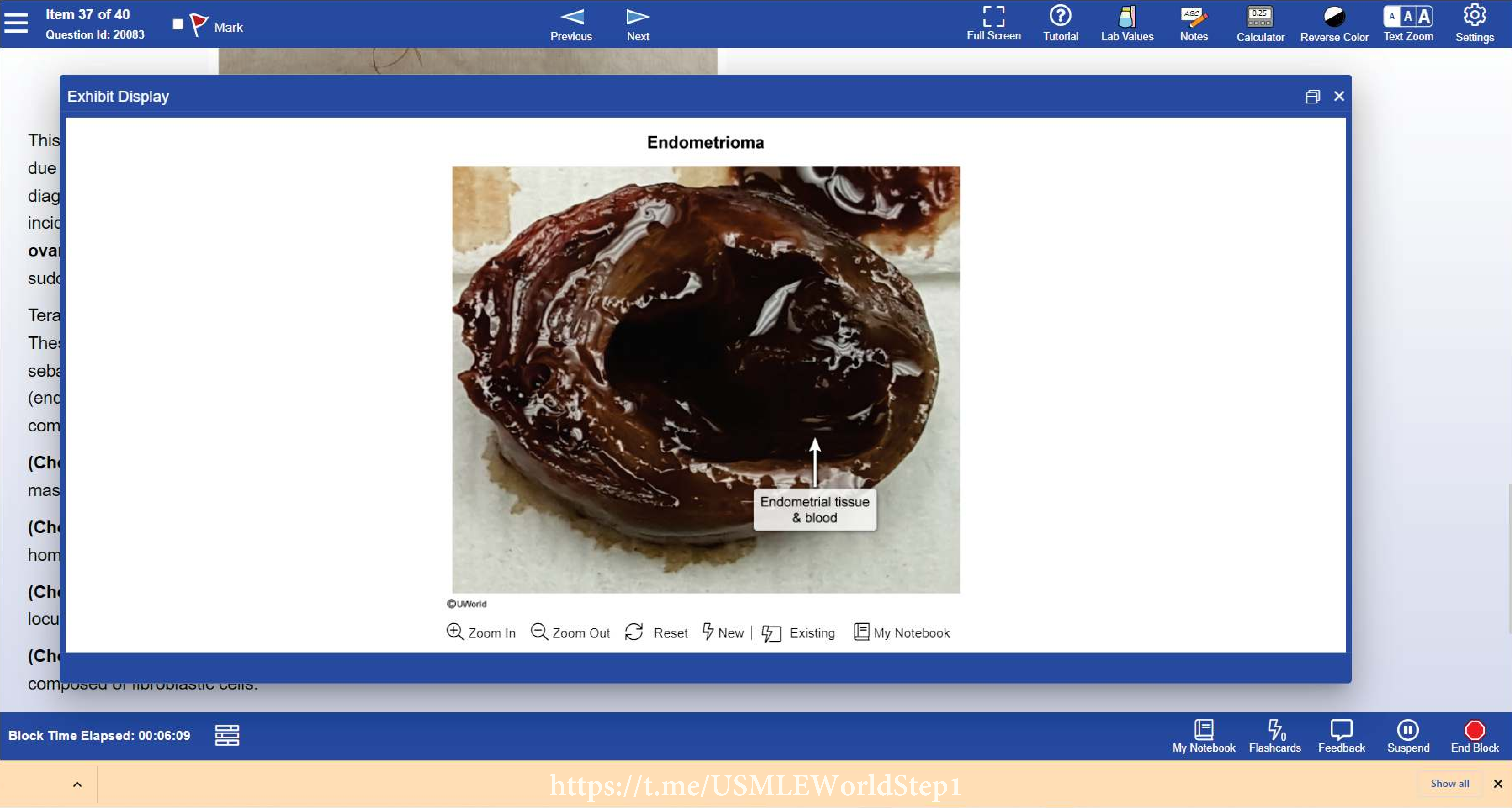
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Endometrioma

Endometrial tissue & blood

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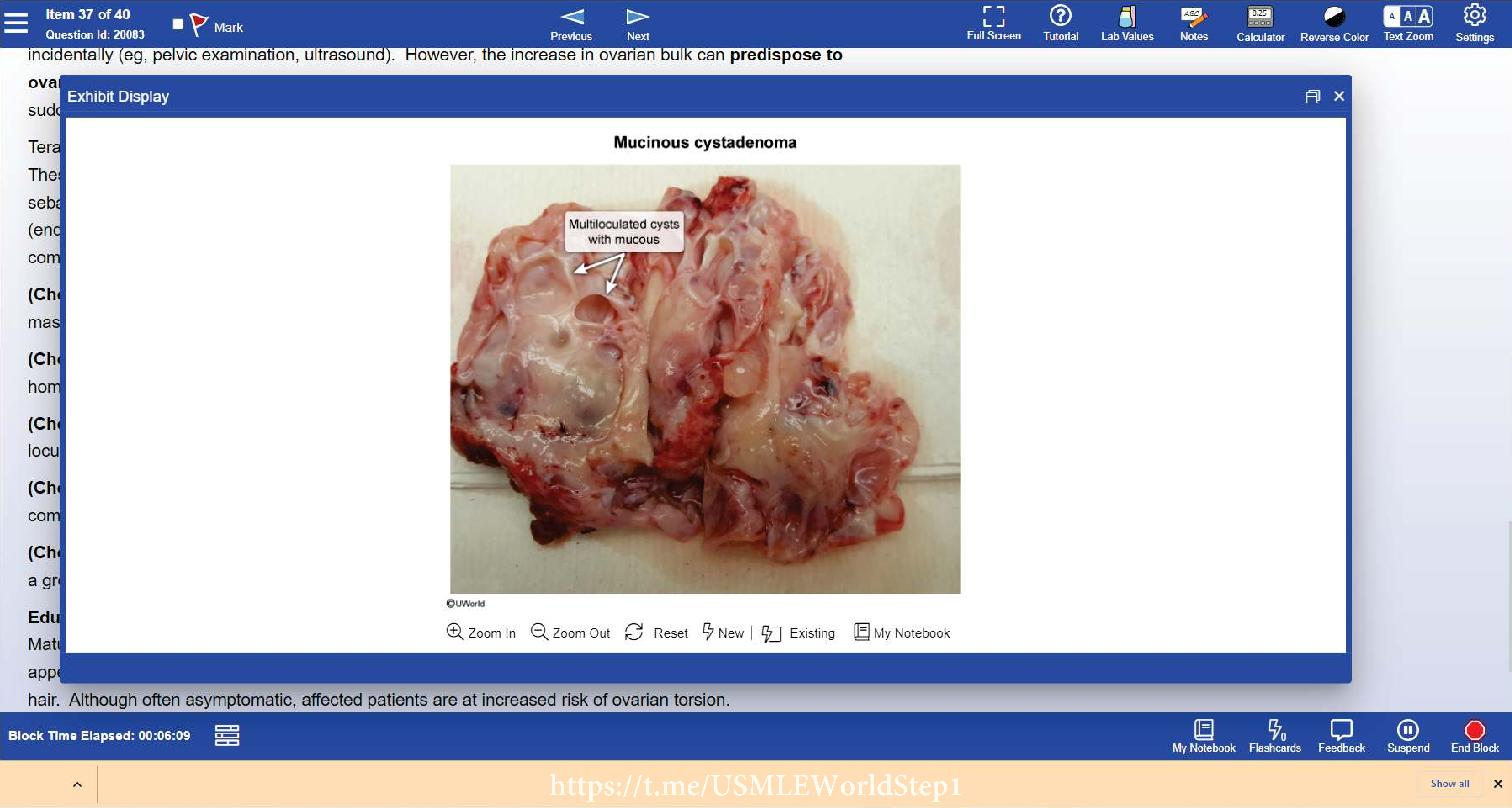
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incidentally (eg, pelvic examination, ultrasound). However, the increase in ovarian bulk can **predispose to ova**

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hair. Although often asymptomatic, affected patients are at increased risk of ovarian torsion.

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Mucinous cystadenoma

Multiloculated cysts with mucous

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Teratomas have a gross appearance consistent with **all 3 germ cell layers** (ectoderm, mesoderm, endoderm).

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- Bilateral dermoid ovarian torsion in a young woman: a case report.

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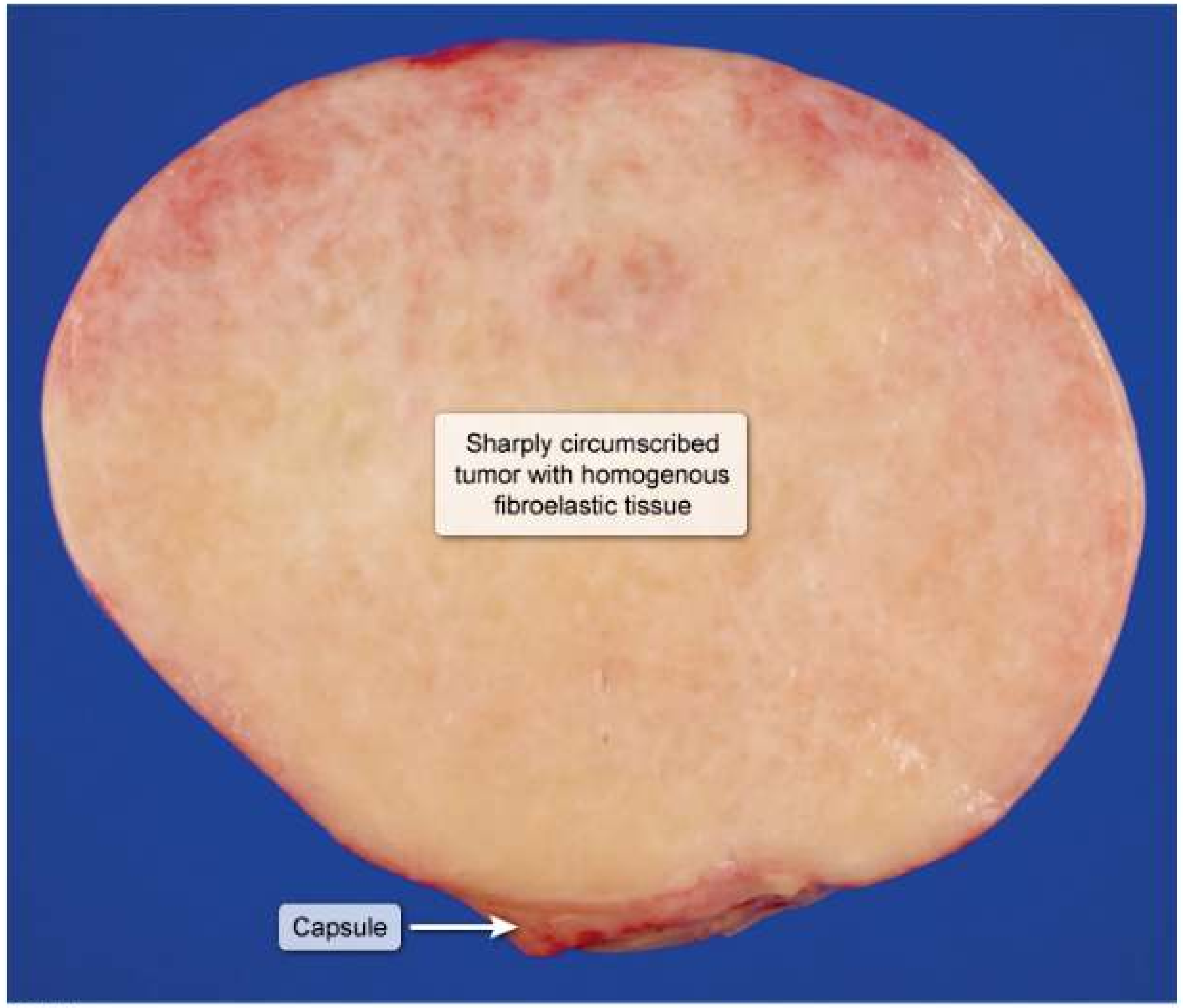
Ovarian fibroma


Sharply circumscribed tumor with homogenous fibroelastic tissue
Capsule

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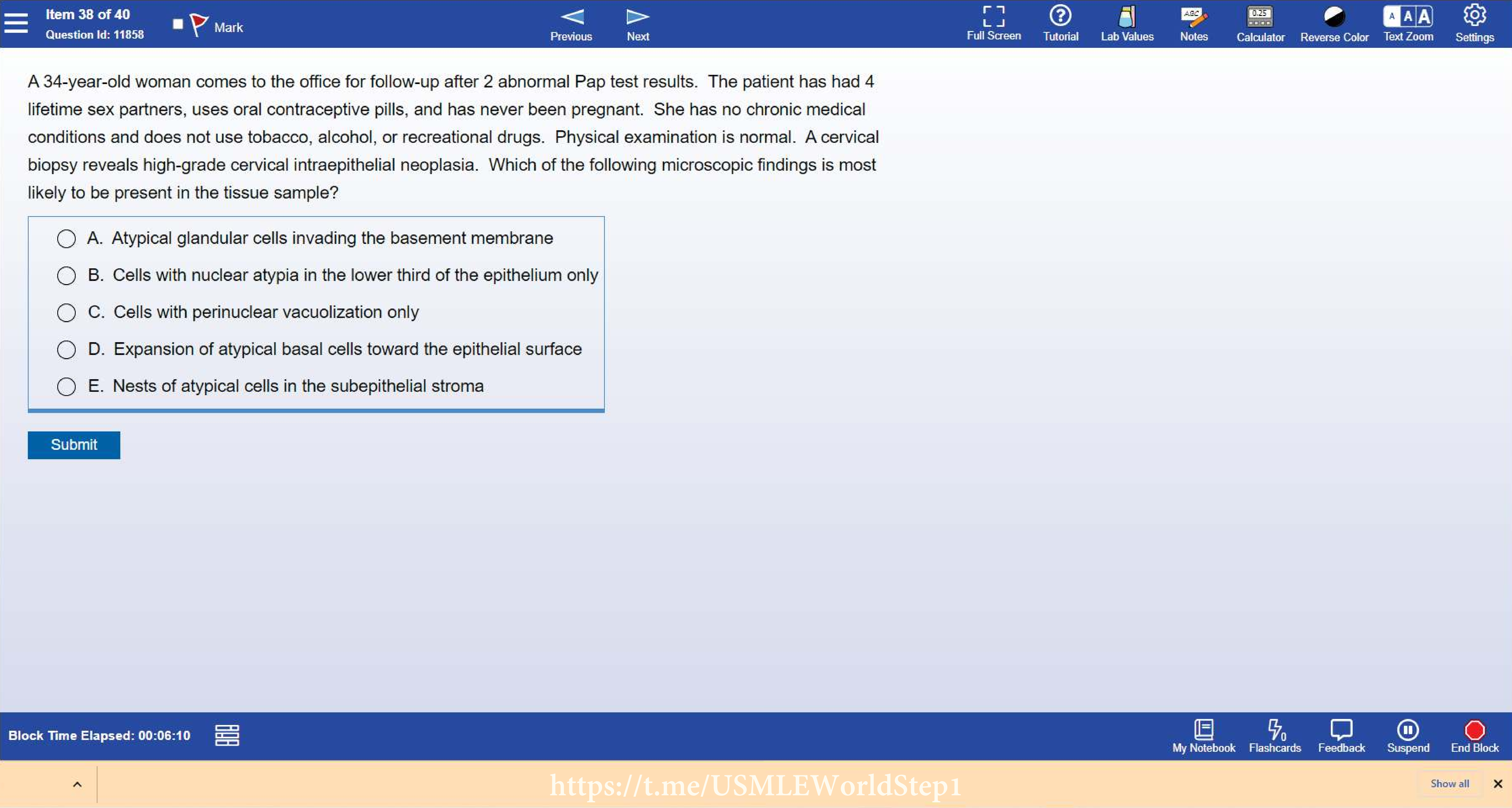
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A 34-year-old woman comes to the office for follow-up after 2 abnormal Pap test results. The patient has had 4 lifetime sex partners, uses oral contraceptive pills, and has never been pregnant. She has no chronic medical conditions and does not use tobacco, alcohol, or recreational drugs. Physical examination is normal. A cervical biopsy reveals high-grade cervical intraepithelial neoplasia. Which of the following microscopic findings is most likely to be present in the tissue sample?

○ A. Atypical glandular cells invading the basement membrane
○ B. Cells with nuclear atypia in the lower third of the epithelium only
○ C. Cells with perinuclear vacuolization only
○ D. Expansion of atypical basal cells toward the epithelial surface
○ E. Nests of atypical cells in the subepithelial stroma

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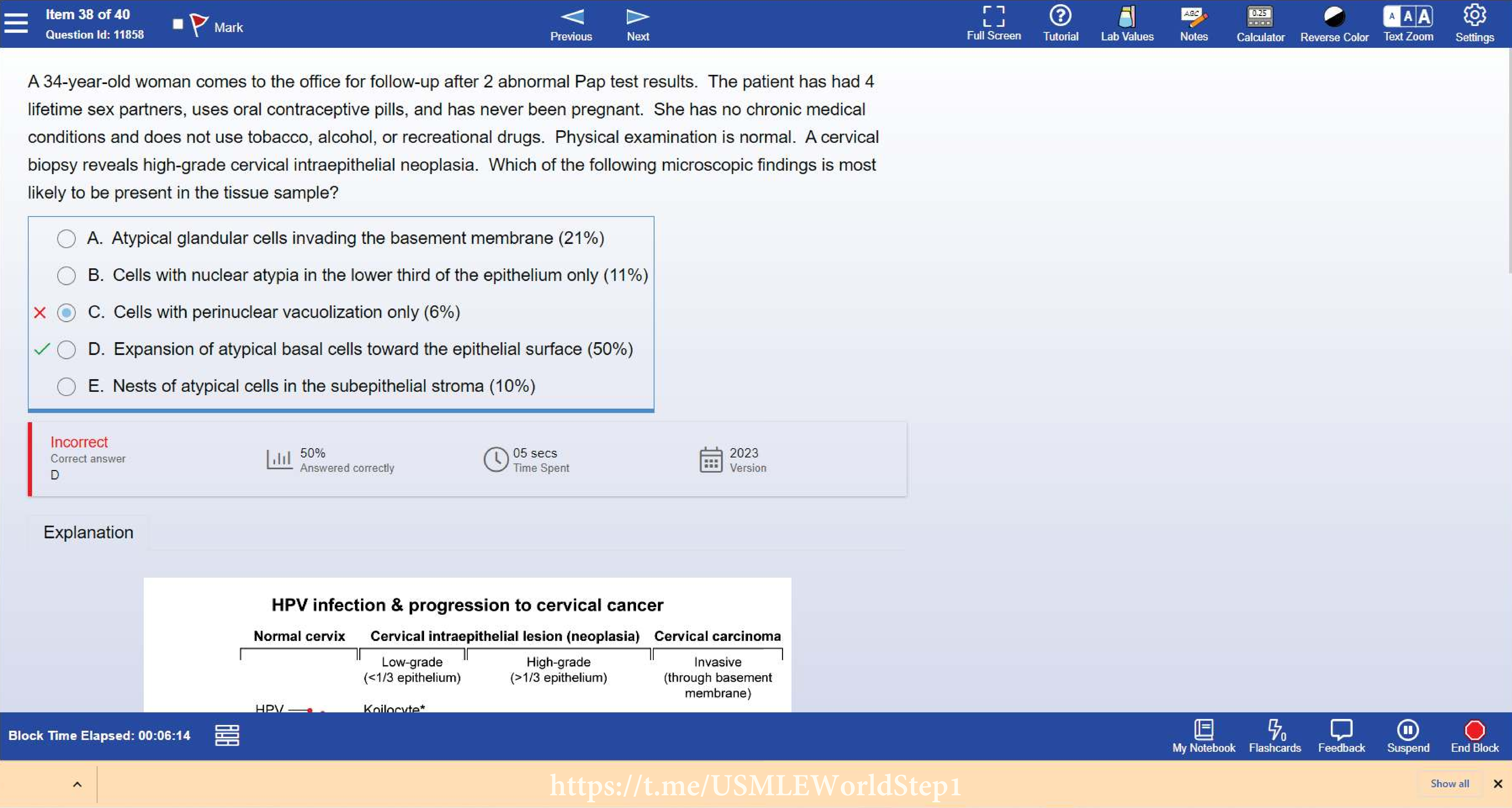

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○ A. Atypical glandular cells invading the basement membrane (21%)
○ B. Cells with nuclear atypia in the lower third of the epithelium only (11%)
✗ ● C. Cells with perinuclear vacuolization only (6%)
✓ ○ D. Expansion of atypical basal cells toward the epithelial surface (50%)
○ E. Nests of atypical cells in the subepithelial stroma (10%)

Incorrect
Correct answer
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50%
Answered correctly

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Explanation

HPV infection & progression to cervical cancer

Normal cervix	Cervical intraepithelial lesion (neoplasia)		Cervical carcinoma
	Low-grade (<1/3 epithelium)	High-grade (>1/3 epithelium)	Invasive (through basement membrane)
HPV	Koilocyte*		

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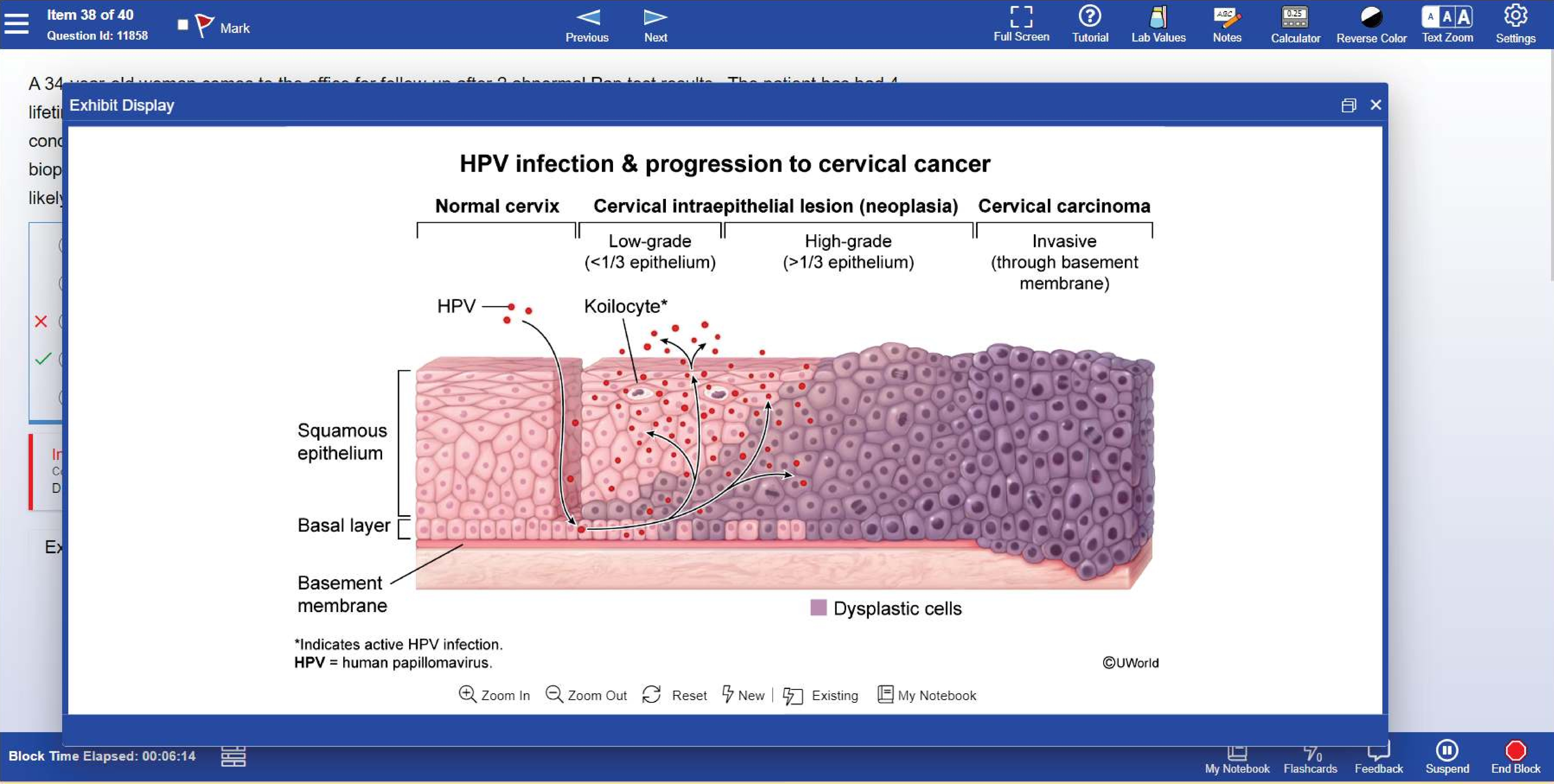
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Squamous epithelium
Basal layer
Basement membrane
HPV
Koilocyte*
Dysplastic cells
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HPV infection & progression to cervical cancer

Normal cervix	Cervical intraepithelial lesion (neoplasia)		Cervical carcinoma
	Low-grade (<1/3 epithelium)	High-grade (>1/3 epithelium)	Invasive (through basement membrane)

*Indicates active HPV infection.

HPV = human papillomavirus.

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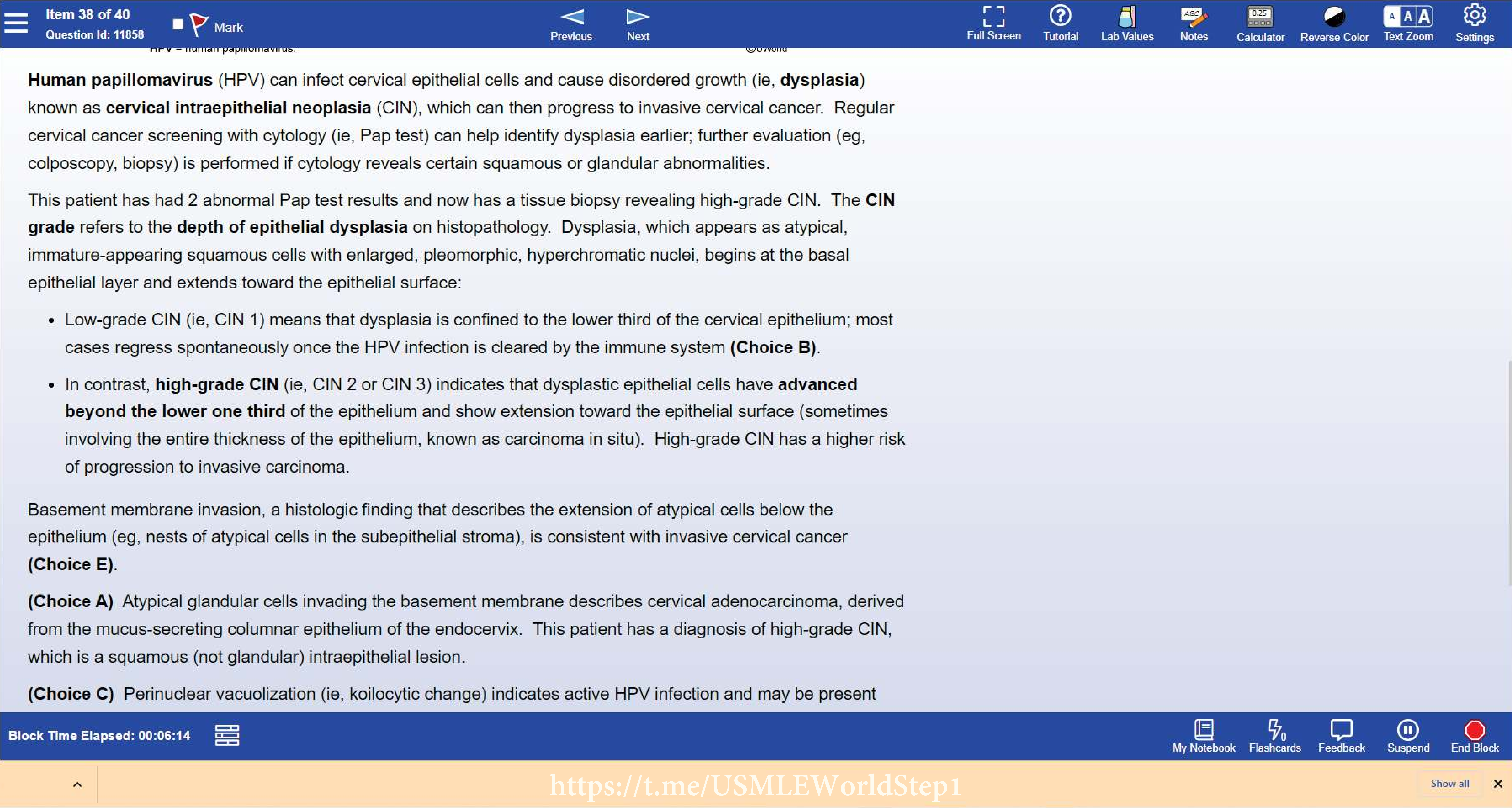


HPV = human papillomavirus. ©UWorld

Human papillomavirus (HPV) can infect cervical epithelial cells and cause disordered growth (ie, **dysplasia**) known as **cervical intraepithelial neoplasia** (CIN), which can then progress to invasive cervical cancer. Regular cervical cancer screening with cytology (ie, Pap test) can help identify dysplasia earlier; further evaluation (eg, colposcopy, biopsy) is performed if cytology reveals certain squamous or glandular abnormalities.

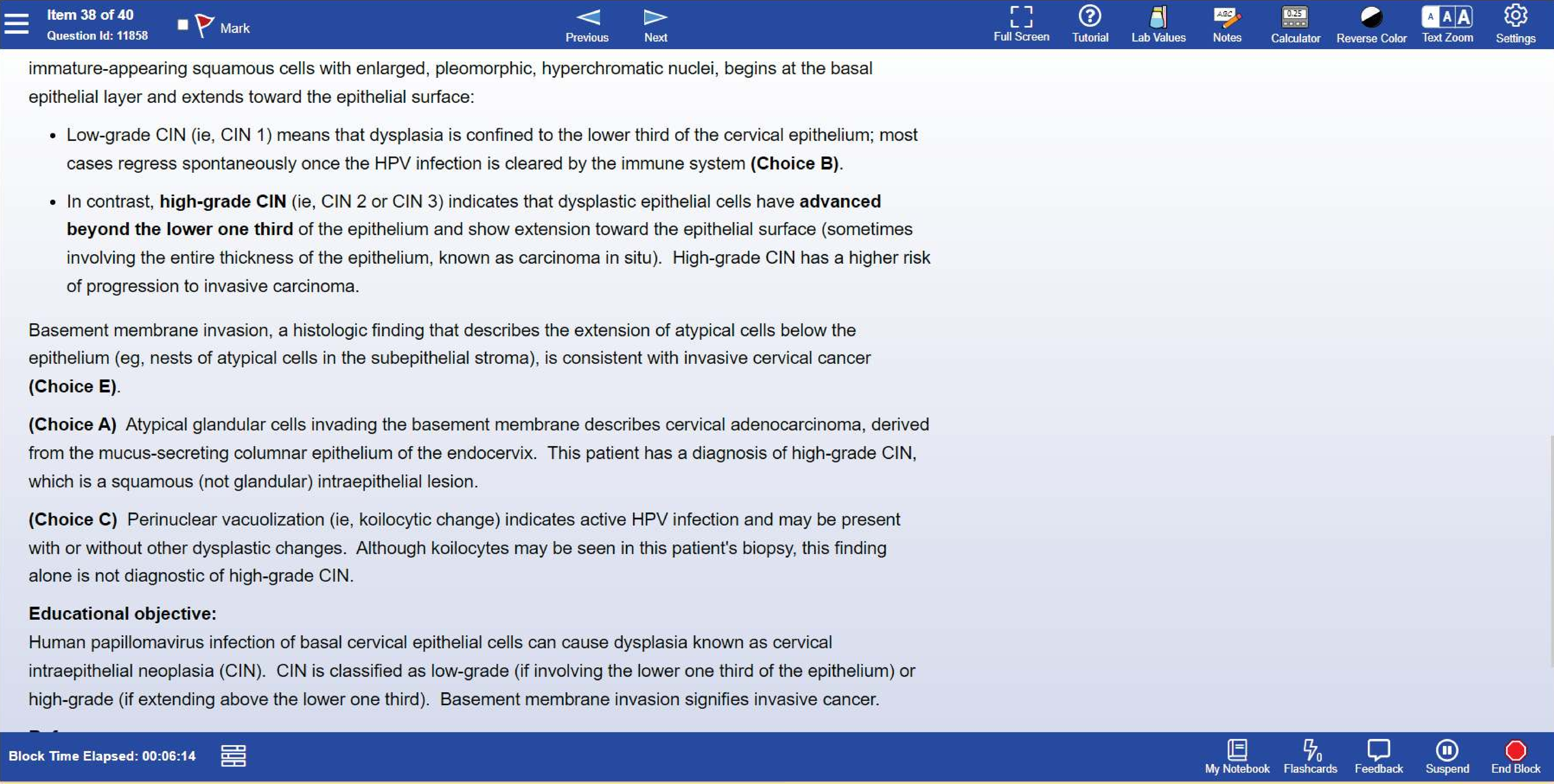
This patient has had 2 abnormal Pap test results and now has a tissue biopsy revealing high-grade CIN. The **CIN grade** refers to the **depth of epithelial dysplasia** on histopathology. Dysplasia, which appears as atypical, immature-appearing squamous cells with enlarged, pleomorphic, hyperchromatic nuclei, begins at the basal epithelial layer and extends toward the epithelial surface:

- Low-grade CIN (ie, CIN 1) means that dysplasia is confined to the lower third of the cervical epithelium; most cases regress spontaneously once the HPV infection is cleared by the immune system **(Choice B)**.
- In contrast, **high-grade CIN** (ie, CIN 2 or CIN 3) indicates that dysplastic epithelial cells have **advanced beyond the lower one third** of the epithelium and show extension toward the epithelial surface (sometimes involving the entire thickness of the epithelium, known as carcinoma in situ). High-grade CIN has a higher risk of progression to invasive carcinoma.

Basement membrane invasion, a histologic finding that describes the extension of atypical cells below the epithelium (eg, nests of atypical cells in the subepithelial stroma), is consistent with invasive cervical cancer **(Choice E)**.

(Choice A) Atypical glandular cells invading the basement membrane describes cervical adenocarcinoma, derived from the mucus-secreting columnar epithelium of the endocervix. This patient has a diagnosis of high-grade CIN, which is a squamous (not glandular) intraepithelial lesion.

(Choice C) Perinuclear vacuolization (ie, koilocytic change) indicates active HPV infection and may be present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immature-appearing squamous cells with enlarged, pleomorphic, hyperchromatic nuclei, begins at the basal epithelial layer and extends toward the epithelial surface:

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(Choice A) Atypical glandular cells invading the basement membrane describes cervical adenocarcinoma, derived from the mucus-secreting columnar epithelium of the endocervix. This patient has a diagnosis of high-grade CIN, which is a squamous (not glandular) intraepithelial lesion.

(Choice C) Perinuclear vacuolization (ie, koilocytic change) indicates active HPV infection and may be present with or without other dysplastic changes. Although koilocytes may be seen in this patient's biopsy, this finding alone is not diagnostic of high-grade CIN.

Educational objective:
Human papillomavirus infection of basal cervical epithelial cells can cause dysplasia known as cervical intraepithelial neoplasia (CIN). CIN is classified as low-grade (if involving the lower one third of the epithelium) or high-grade (if extending above the lower one third). Basement membrane invasion signifies invasive cancer.

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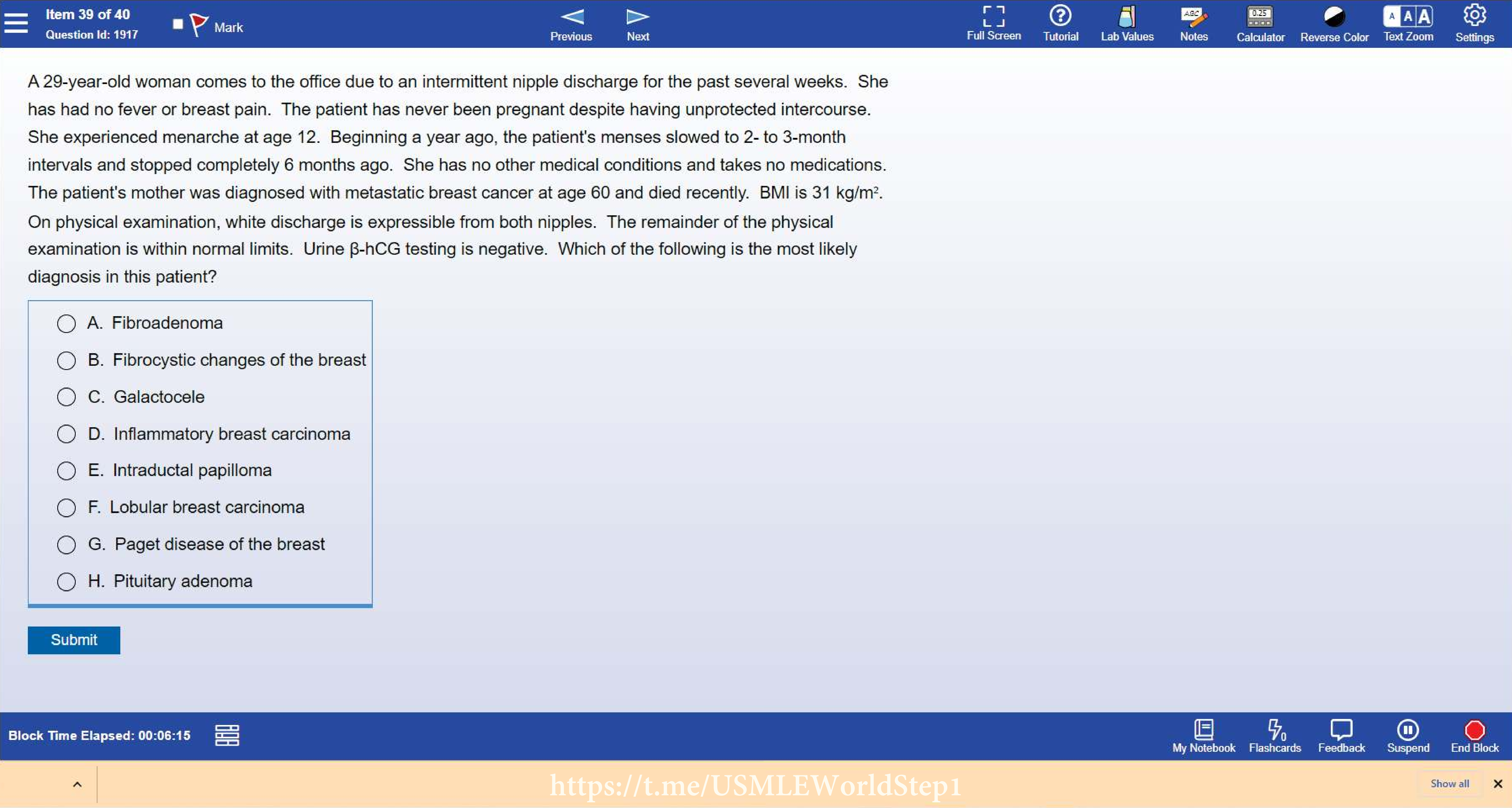
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A 29-year-old woman comes to the office due to an intermittent nipple discharge for the past several weeks. She has had no fever or breast pain. The patient has never been pregnant despite having unprotected intercourse. She experienced menarche at age 12. Beginning a year ago, the patient's menses slowed to 2- to 3-month intervals and stopped completely 6 months ago. She has no other medical conditions and takes no medications. The patient's mother was diagnosed with metastatic breast cancer at age 60 and died recently. BMI is 31 kg/m^2. On physical examination, white discharge is expressible from both nipples. The remainder of the physical examination is within normal limits. Urine β-hCG testing is negative. Which of the following is the most likely diagnosis in this patient?

- ○ A. Fibroadenoma
- ○ B. Fibrocystic changes of the breast
- ○ C. Galactocele
- ○ D. Inflammatory breast carcinoma
- ○ E. Intraductal papilloma
- ○ F. Lobular breast carcinoma
- ○ G. Paget disease of the breast
- ○ H. Pituitary adenoma

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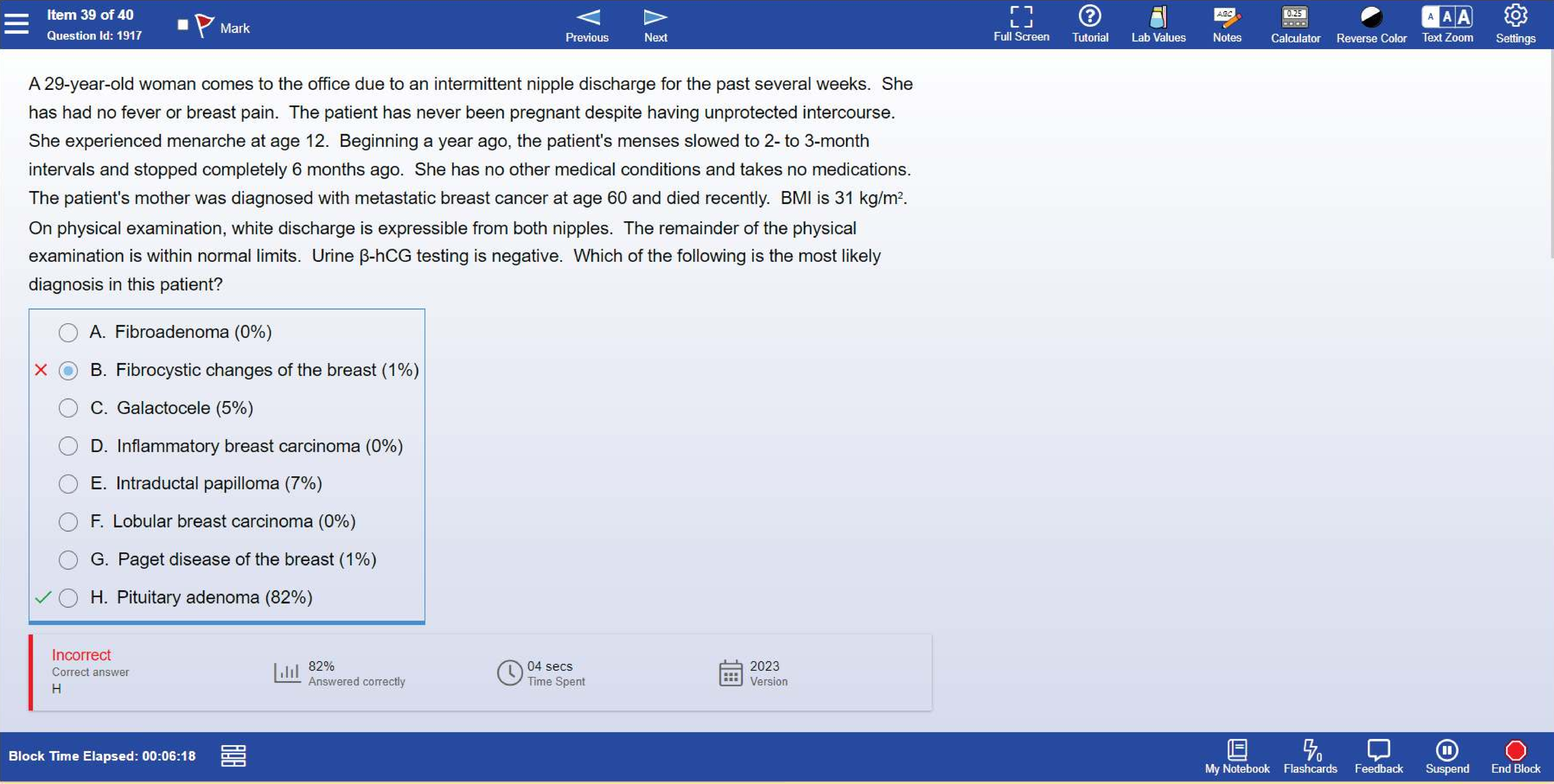
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○ A. Fibroadenoma (0%)
✗ ● B. Fibrocystic changes of the breast (1%)
○ C. Galactocele (5%)
○ D. Inflammatory breast carcinoma (0%)
○ E. Intraductal papilloma (7%)
○ F. Lobular breast carcinoma (0%)
○ G. Paget disease of the breast (1%)
✓ ○ H. Pituitary adenoma (82%)

Incorrect
Correct answer
H

82%
Answered correctly

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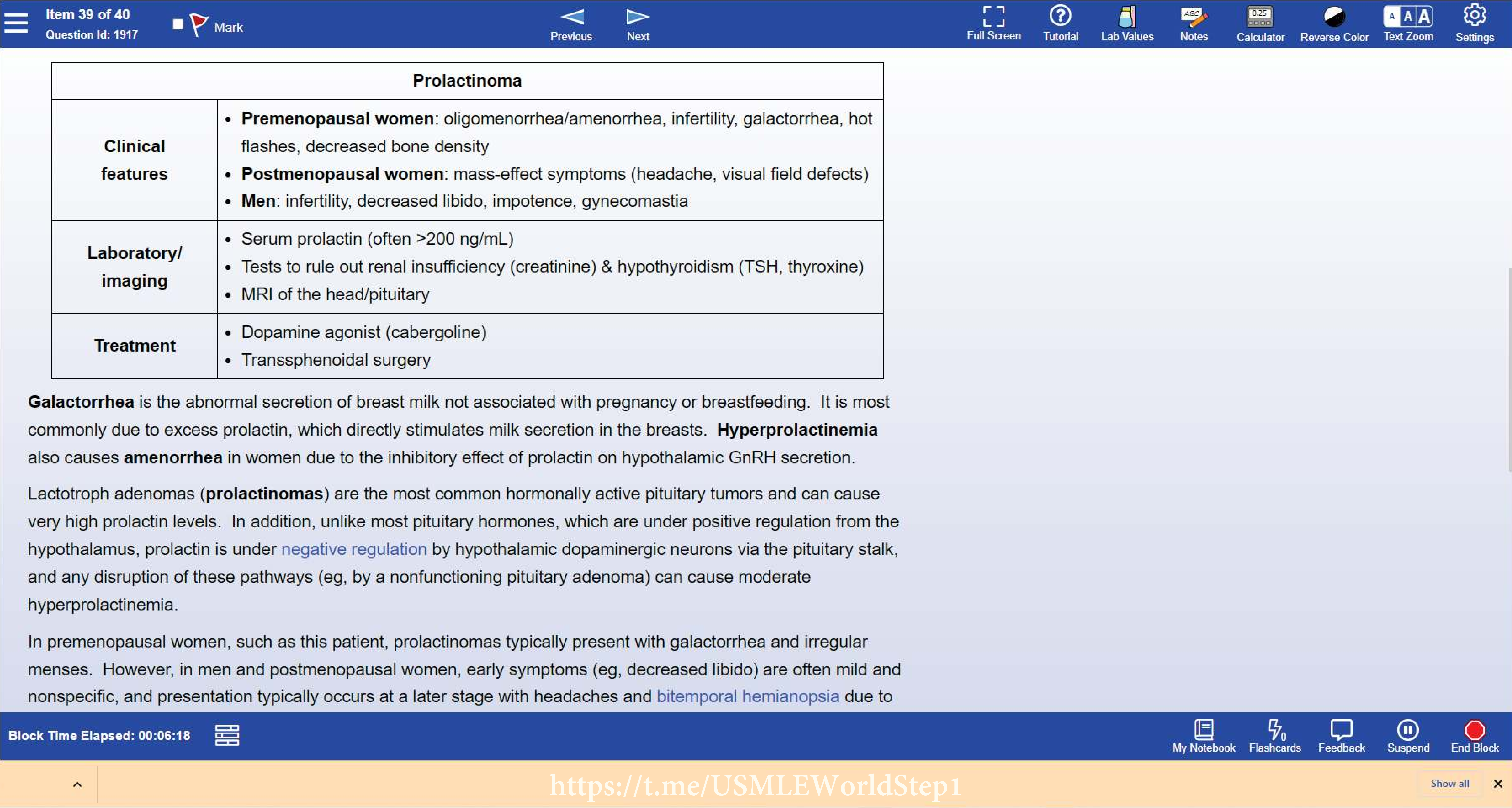
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Prolactinoma	
Clinical features	• **Premenopausal women**: oligomenorrhea/amenorrhea, infertility, galactorrhea, hot flashes, decreased bone density • **Postmenopausal women**: mass-effect symptoms (headache, visual field defects) • **Men**: infertility, decreased libido, impotence, gynecomastia
Laboratory/ imaging	• Serum prolactin (often >200 ng/mL) • Tests to rule out renal insufficiency (creatinine) & hypothyroidism (TSH, thyroxine) • MRI of the head/pituitary
Treatment	• Dopamine agonist (cabergoline) • Transsphenoidal surgery

Galactorrhea is the abnormal secretion of breast milk not associated with pregnancy or breastfeeding. It is most commonly due to excess prolactin, which directly stimulates milk secretion in the breasts. **Hyperprolactinemia** also causes **amenorrhea** in women due to the inhibitory effect of prolactin on hypothalamic GnRH secretion.

Lactotroph adenomas (**prolactinomas**) are the most common hormonally active pituitary tumors and can cause very high prolactin levels. In addition, unlike most pituitary hormones, which are under positive regulation from the hypothalamus, prolactin is under negative regulation by hypothalamic dopaminergic neurons via the pituitary stalk, and any disruption of these pathways (eg, by a nonfunctioning pituitary adenoma) can cause moderate hyperprolactinemia.

In premenopausal women, such as this patient, prolactinomas typically present with galactorrhea and irregular menses. However, in men and postmenopausal women, early symptoms (eg, decreased libido) are often mild and nonspecific, and presentation typically occurs at a later stage with headaches and bitemporal hemianopsia due to

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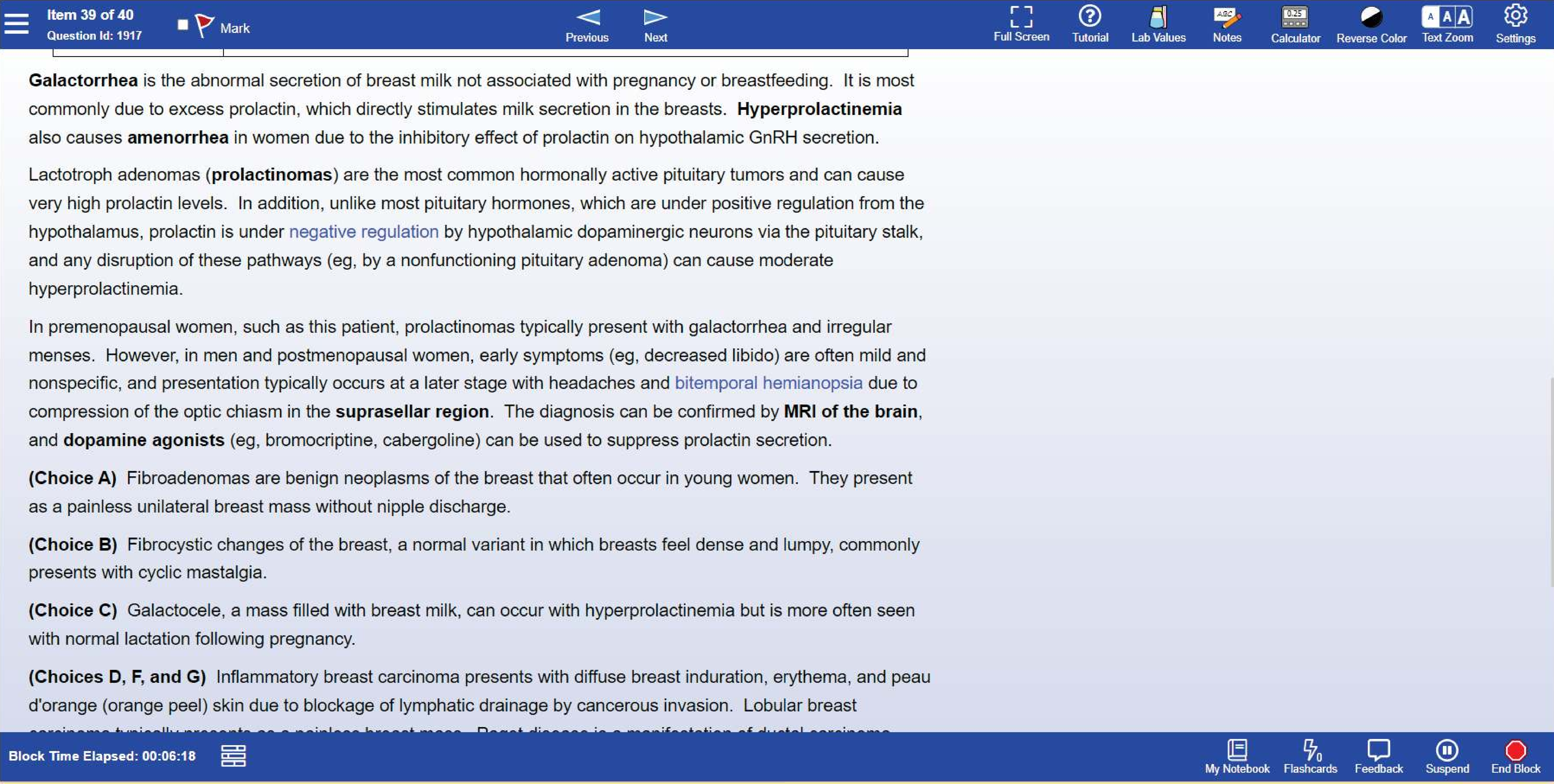

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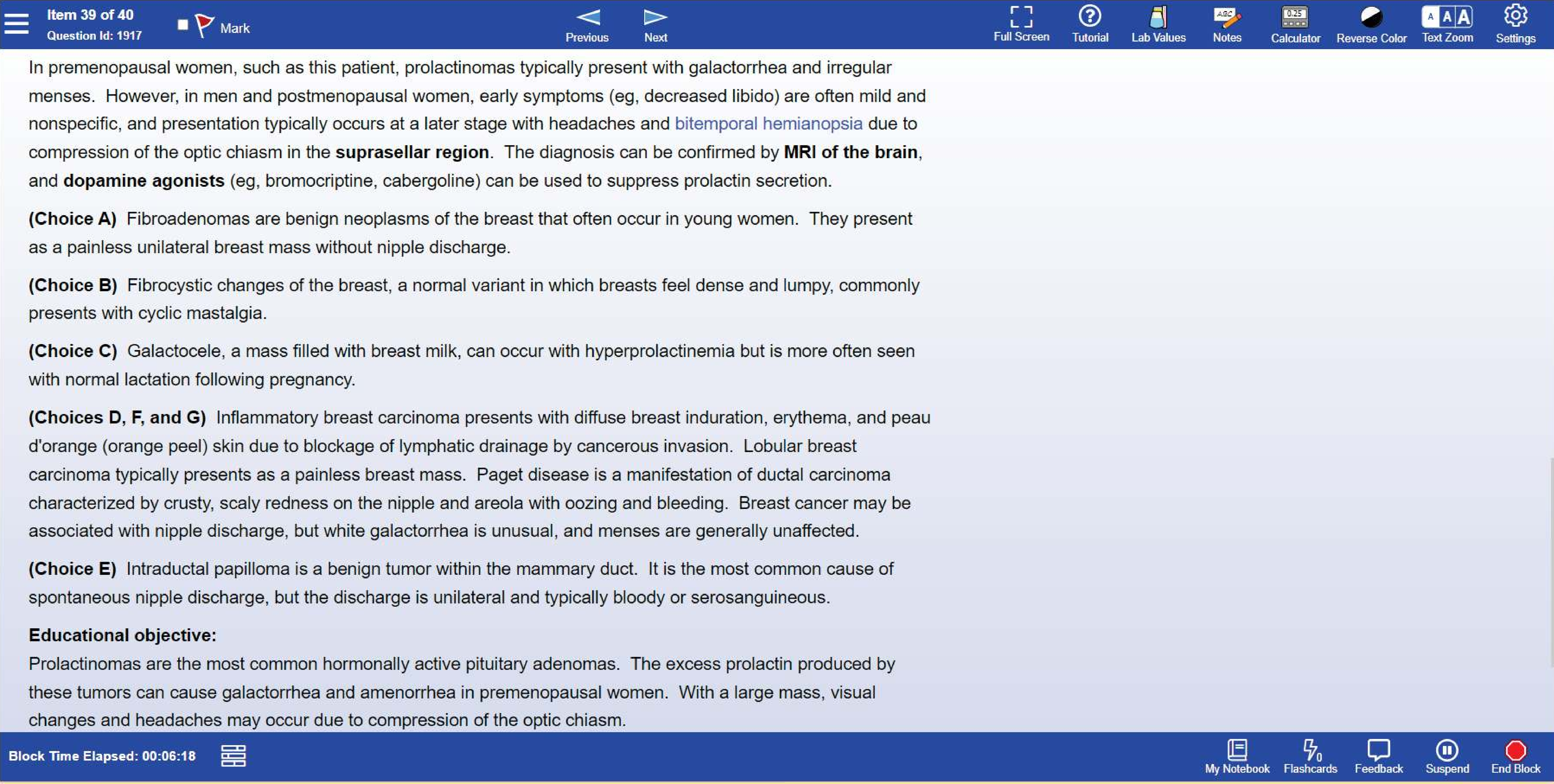
In premenopausal women, such as this patient, prolactinomas typically present with galactorrhea and irregular menses. However, in men and postmenopausal women, early symptoms (eg, decreased libido) are often mild and nonspecific, and presentation typically occurs at a later stage with headaches and bitemporal hemianopsia due to compression of the optic chiasm in the **suprasellar region**. The diagnosis can be confirmed by **MRI of the brain**, and **dopamine agonists** (eg, bromocriptine, cabergoline) can be used to suppress prolactin secretion.

(Choice A) Fibroadenomas are benign neoplasms of the breast that often occur in young women. They present as a painless unilateral breast mass without nipple discharge.

(Choice B) Fibrocystic changes of the breast, a normal variant in which breasts feel dense and lumpy, commonly presents with cyclic mastalgia.

(Choice C) Galactocele, a mass filled with breast milk, can occur with hyperprolactinemia but is more often seen with normal lactation following pregnancy.

(Choices D, F, and G) Inflammatory breast carcinoma presents with diffuse breast induration, erythema, and peau d'orange (orange peel) skin due to blockage of lymphatic drainage by cancerous invasion. Lobular breast carcinoma typically presents as a painless breast mass. Paget disease is a manifestation of ductal carcinoma



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(Choice E) Intraductal papilloma is a benign tumor within the mammary duct. It is the most common cause of spontaneous nipple discharge, but the discharge is unilateral and typically bloody or serosanguineous.

Educational objective:
Prolactinomas are the most common hormonally active pituitary adenomas. The excess prolactin produced by these tumors can cause galactorrhea and amenorrhea in premenopausal women. With a large mass, visual changes and headaches may occur due to compression of the optic chiasm.

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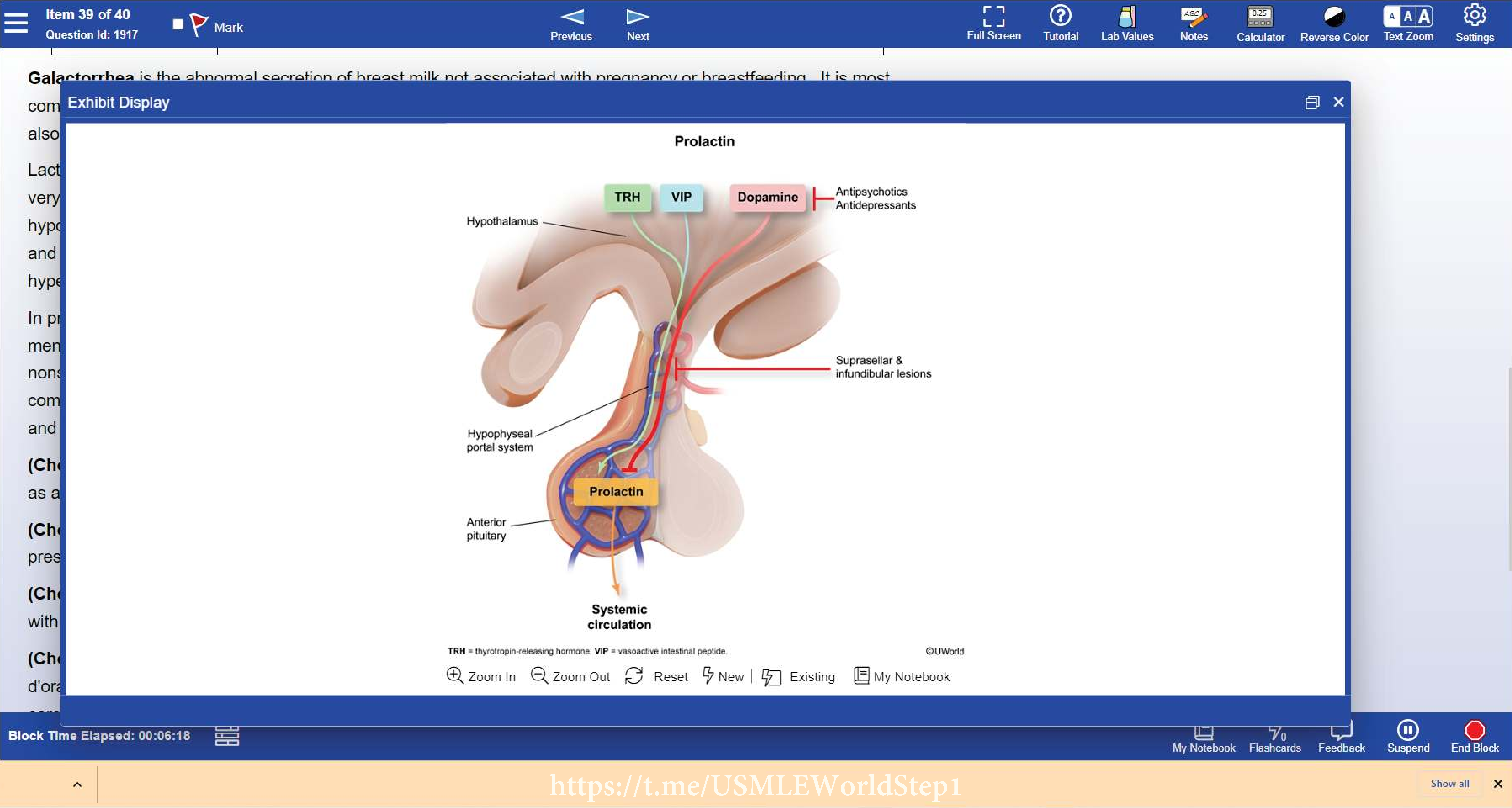
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Galactorrhea is the abnormal secretion of breast milk not associated with pregnancy or breastfeeding. It is most

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Prolactin

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Suprasellar &
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Hypophyseal
portal system
Prolactin
Anterior
pituitary
Systemic
circulation

TRH = thyrotropin-releasing hormone; **VIP** = vasoactive intestinal peptide.

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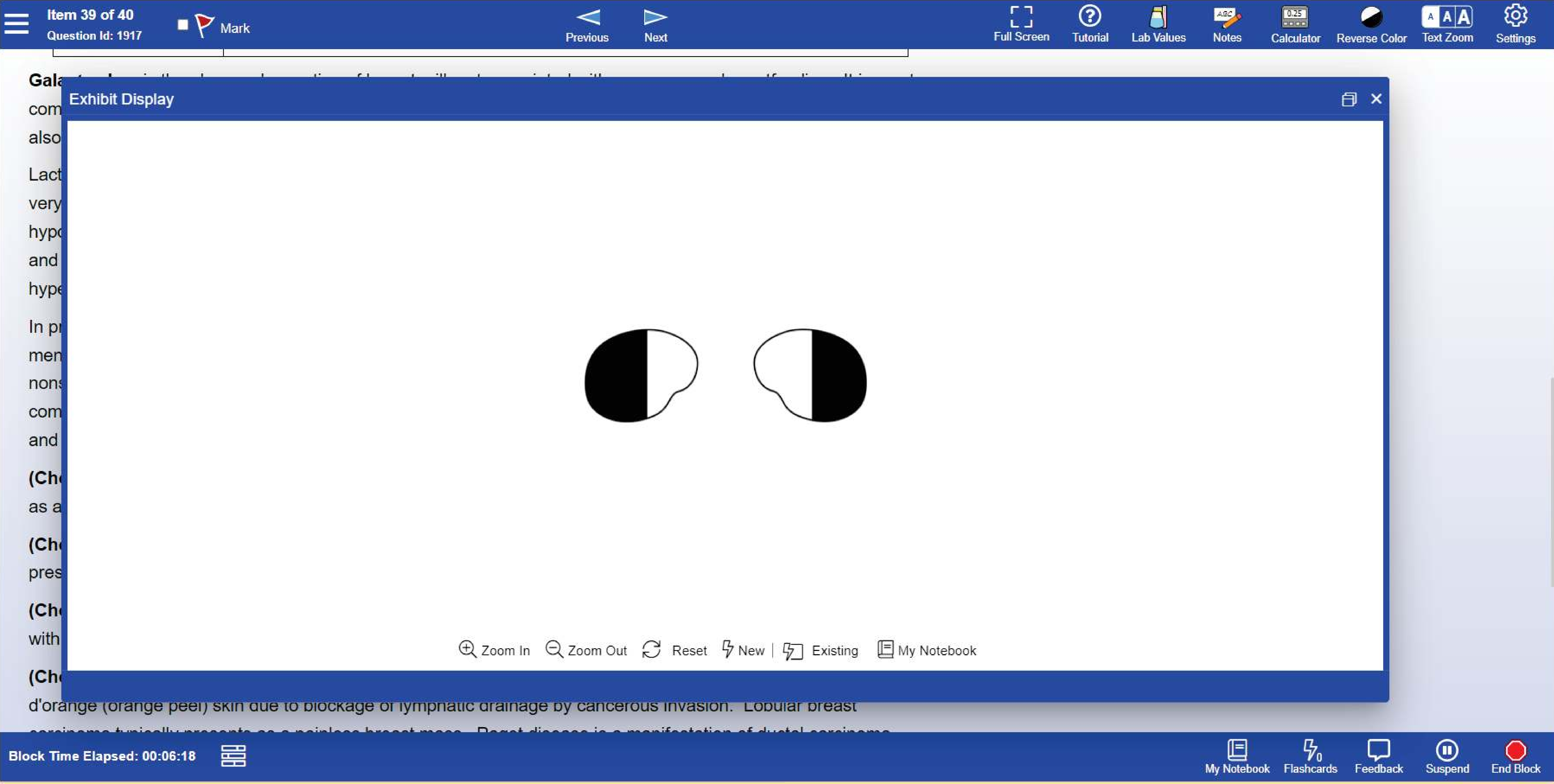
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d'orange (orange peel) skin due to blockage of lymphatic drainage by cancerous invasion. Lobular breast

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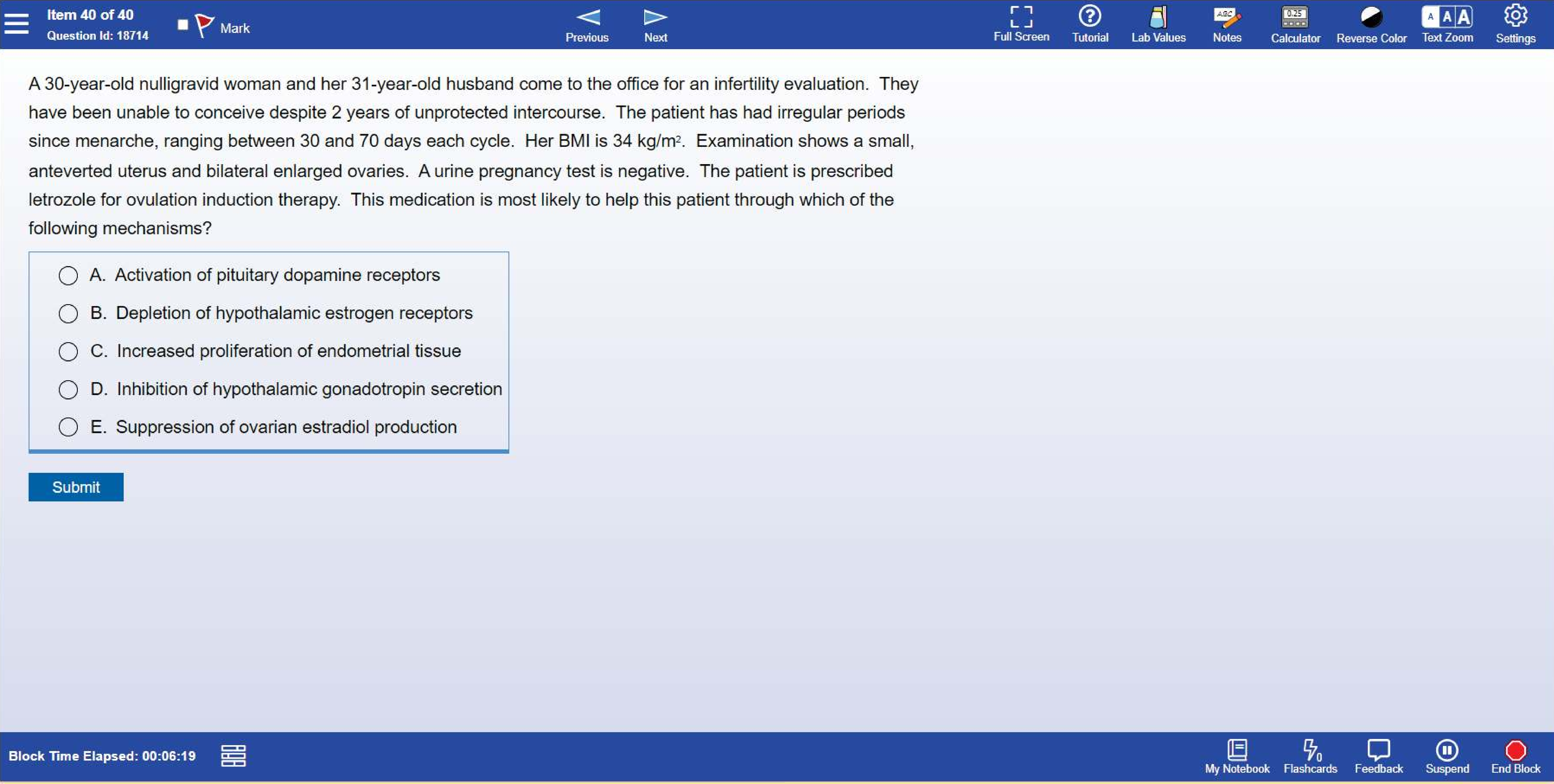
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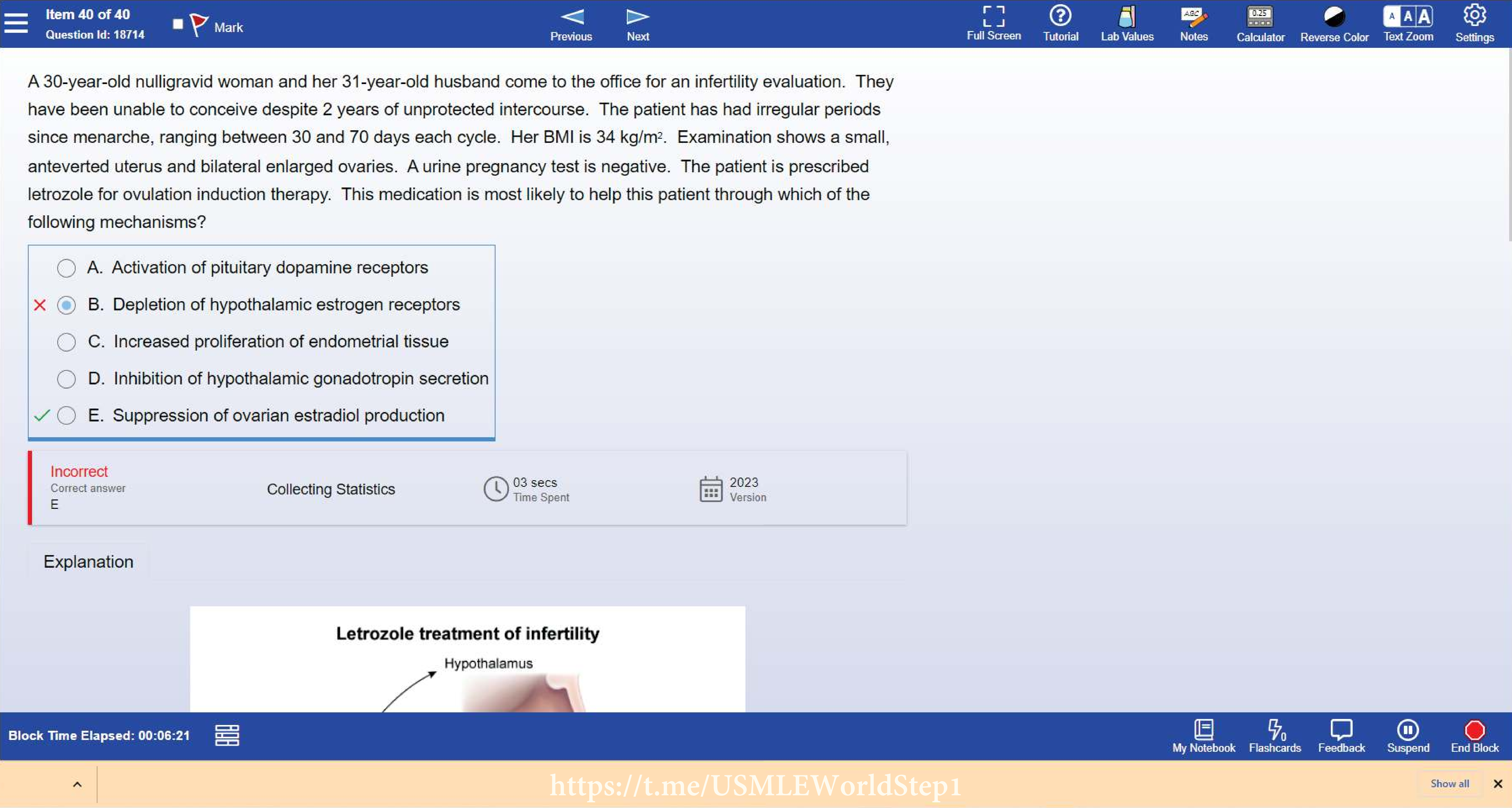
A 30-year-old nulligravid woman and her 31-year-old husband come to the office for an infertility evaluation. They have been unable to conceive despite 2 years of unprotected intercourse. The patient has had irregular periods since menarche, ranging between 30 and 70 days each cycle. Her BMI is 34 kg/m^2. Examination shows a small, anteverted uterus and bilateral enlarged ovaries. A urine pregnancy test is negative. The patient is prescribed letrozole for ovulation induction therapy. This medication is most likely to help this patient through which of the following mechanisms?

○ A. Activation of pituitary dopamine receptors
○ B. Depletion of hypothalamic estrogen receptors
○ C. Increased proliferation of endometrial tissue
○ D. Inhibition of hypothalamic gonadotropin secretion
○ E. Suppression of ovarian estradiol production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- ✓ ○ E. Suppression of ovarian estradiol production

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Explanation

Letrozole treatment of infertility

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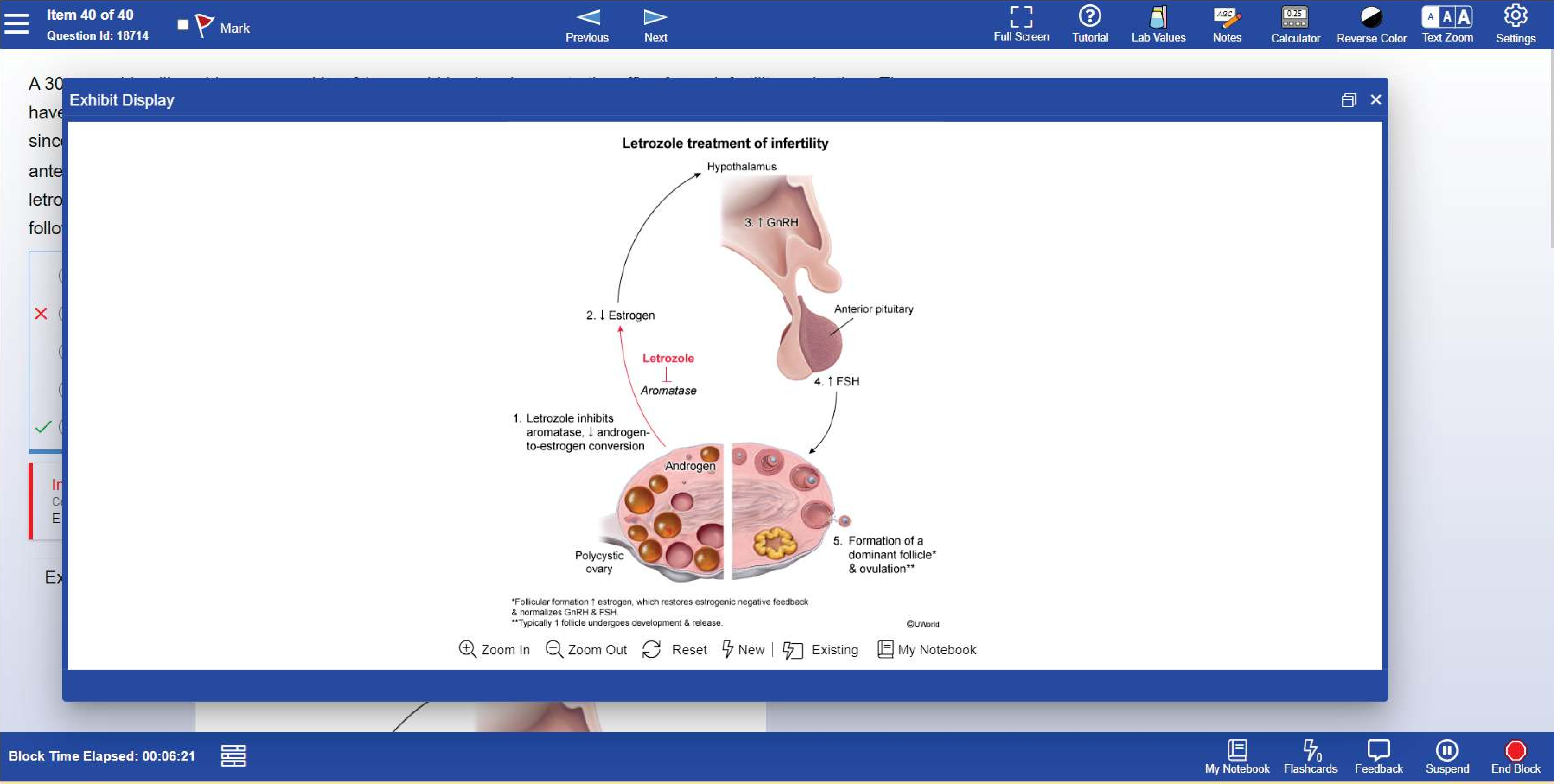
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Letrozole treatment of infertility

Hypothalamus
3. ↑ GnRH
Anterior pituitary
4. ↑ FSH
2. ↓ Estrogen
Letrozole
Aromatase
1. Letrozole inhibits aromatase, ↓ androgen-to-estrogen conversion
Androgen
Polycystic ovary
5. Formation of a dominant follicle* & ovulation**

*Follicular formation ↑ estrogen, which restores estrogenic negative feedback & normalizes GnRH & FSH.
**Typically 1 follicle undergoes development & release.

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& normalizes GnRH & FSH.
**Typically 1 follicle undergoes development & release.

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This patient with irregular menses and enlarged ovaries likely has **polycystic ovary syndrome** (PCOS), a common cause of **infertility** due to anovulation. Ovulation induction agents (eg, letrozole, clomiphene) can be used to treat anovulatory infertility by **increasing gonadotropin levels** (ie, FSH, LH), which stimulates ovulation. Letrozole and clomiphene stimulate gonadotropin release via manipulation of different targets on the hypothalamic-pituitary-ovarian (HPO) axis:

- **Letrozole** acts on the ovary. Patients with PCOS typically have increased ovarian estrogen (eg, estradiol) production, which inhibits FSH, LH, and ovulation. Ovarian estrogen production occurs primarily by the conversion of androgens (produced by theca cells) into estrogens within granulosa cells that contain the enzyme aromatase. Letrozole **inhibits aromatase** (ie, prevents androgen-to-estrogen conversion) and **suppresses ovarian estradiol production**. Letrozole also inhibits aromatase in adipose tissue, decreasing another source of estrogen (eg, estrone). In response, the pituitary releases more FSH and LH, which stimulates ovulation.
- **Clomiphene** acts on estrogen receptors in the hypothalamus and pituitary. When estrogen levels are high (as in PCOS), there is negative estrogenic feedback on both the hypothalamus and pituitary to stop the release of GnRH, FSH, and LH. Clomiphene binds to estrogen receptors for an extended period, resulting in receptor depletion in the hypothalamus and pituitary, thereby allowing for continued FSH and LH release **(Choice B)**.

(Choice A) Bromocriptine, a dopamine receptor agonist, decreases prolactin secretion. Prolactin normally inhibits FSH release, so patients with hyperprolactinemia (eg, lactotroph adenoma) often have infertility. In these patients, bromocriptine can normalize prolactin levels and restore FSH and estrogen levels.

(Choice C) Increased endometrial proliferation, which increases the risk for endometrial hyperplasia or cancer, occurs with the use of unopposed estrogen (eg, estrogen-only hormone therapy) or certain selective estrogen

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(Choice C) Increased endometrial proliferation, which increases the risk for endometrial hyperplasia or cancer, occurs with the use of unopposed estrogen (eg, estrogen-only hormone therapy) or certain selective estrogen receptor modulators (eg, tamoxifen).

(Choice D) When administered continuously, leuprolide (GnRH agonist) downregulates pituitary GnRH receptors and decreases FSH and estrogen, causing a hypogonadotropic, hypogonadal state clinically similar to that of menopause.

Educational objective:

Polycystic ovary syndrome can present with irregular menses, enlarged ovaries, and anovulatory infertility. Letrozole, an aromatase inhibitor, acts on the ovary and peripheral adipose tissue to inhibit androgen-to-estrogen conversion by the enzyme aromatase; the subsequent decrease in estrogen production causes the pituitary to release more FSH and LH, thereby stimulating ovulation.

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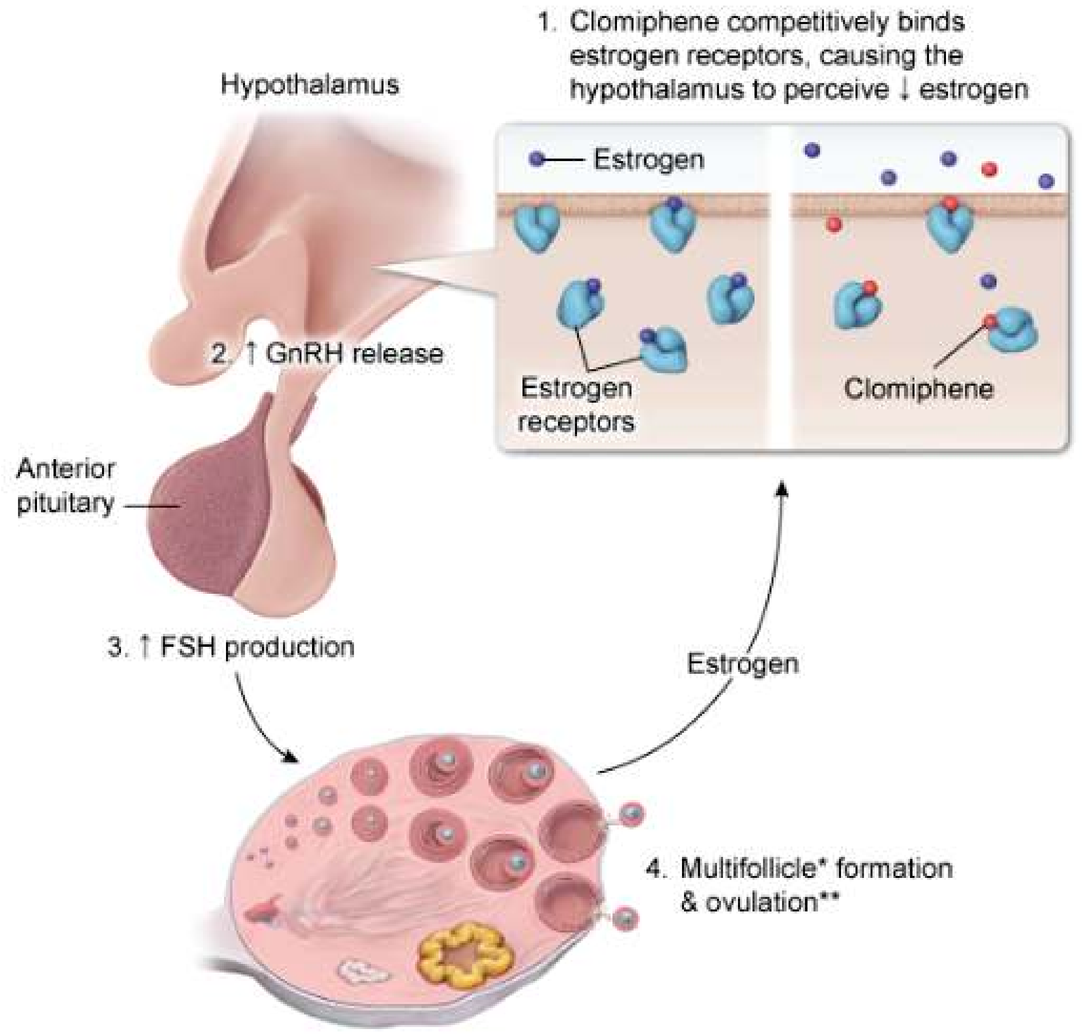
Clomiphene treatment of infertility


1. Clomiphene competitively binds estrogen receptors, causing the hypothalamus to perceive ↓ estrogen
Hypothalamus
Estrogen
Estrogen receptors
Clomiphene
2. ↑ GnRH release
Anterior pituitary
3. ↑ FSH production
Estrogen
4. Multifollicle* formation & ovulation**

*Follicular maturation ↑ estrogen, but clomiphene remains bound to estrogen receptors & causes continued GnRH & FSH release.
**Possible multifollicular development & release.

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bromocriptine can normalize prolactin levels and restore FSH and estrogen levels.

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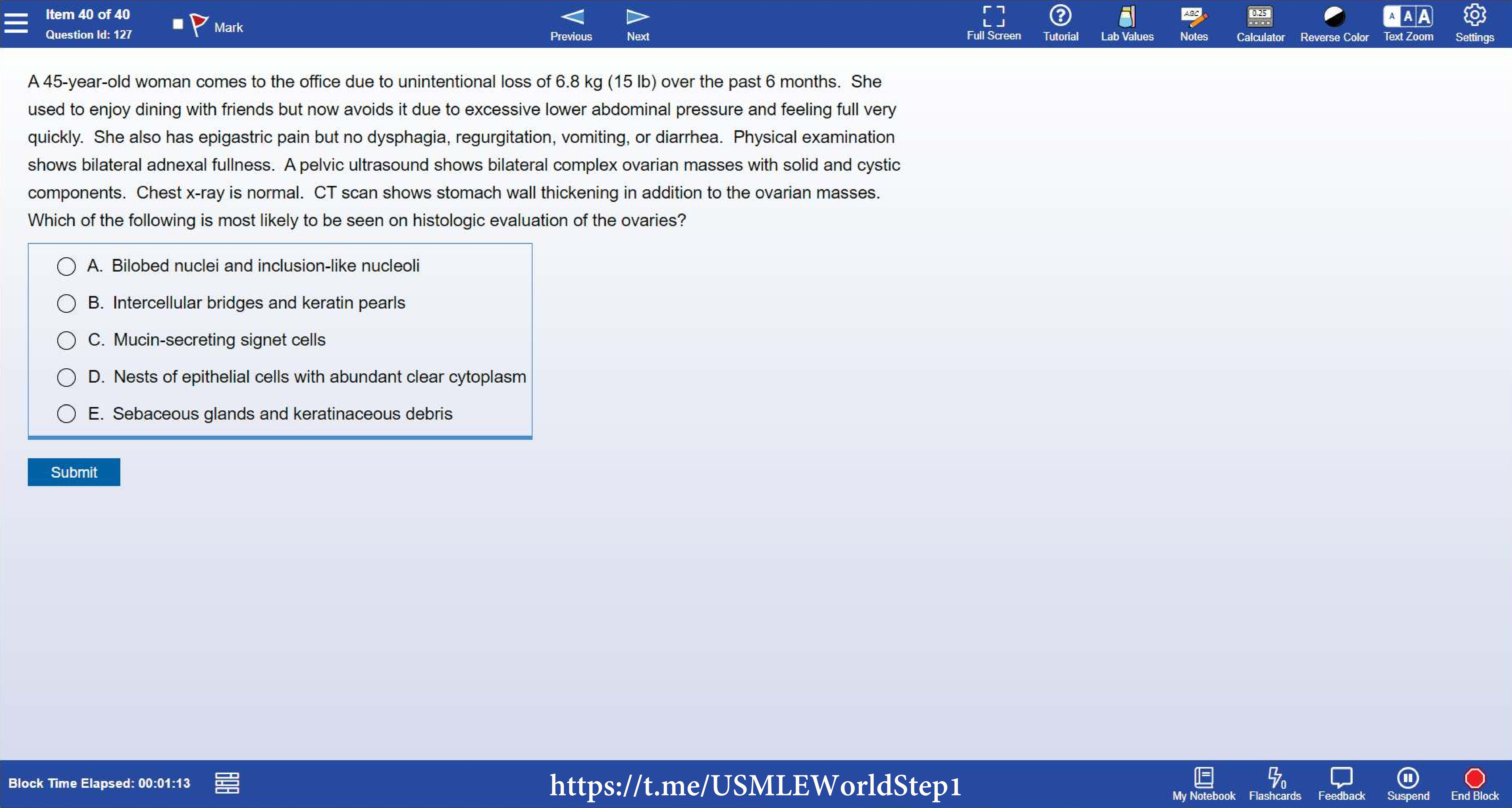
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A 45-year-old woman comes to the office due to unintentional loss of 6.8 kg (15 lb) over the past 6 months. She used to enjoy dining with friends but now avoids it due to excessive lower abdominal pressure and feeling full very quickly. She also has epigastric pain but no dysphagia, regurgitation, vomiting, or diarrhea. Physical examination shows bilateral adnexal fullness. A pelvic ultrasound shows bilateral complex ovarian masses with solid and cystic components. Chest x-ray is normal. CT scan shows stomach wall thickening in addition to the ovarian masses. Which of the following is most likely to be seen on histologic evaluation of the ovaries?

○ A. Bilobed nuclei and inclusion-like nucleoli
○ B. Intercellular bridges and keratin pearls
○ C. Mucin-secreting signet cells
○ D. Nests of epithelial cells with abundant clear cytoplasm
○ E. Sebaceous glands and keratinaceous debris

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○ A. Bilobed nuclei and inclusion-like nucleoli (1%)
○ B. Intercellular bridges and keratin pearls (3%)
✓ ● C. Mucin-secreting signet cells (78%)
○ D. Nests of epithelial cells with abundant clear cytoplasm (10%)
○ E. Sebaceous glands and keratinaceous debris (5%)

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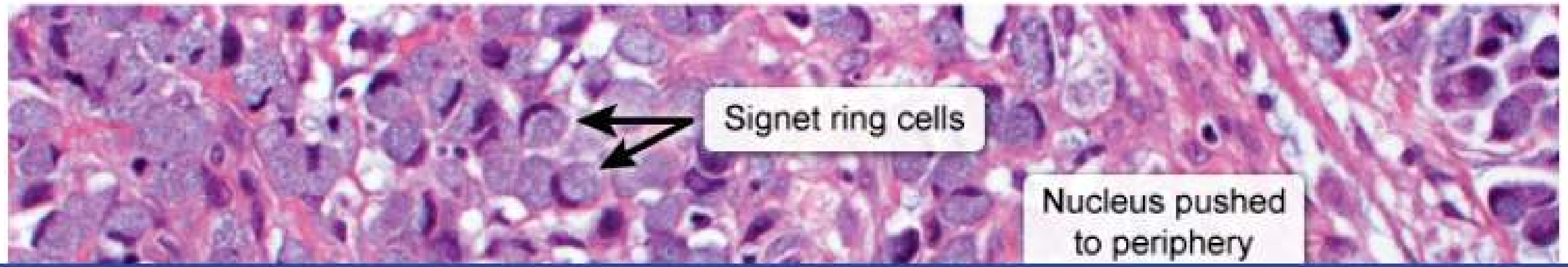
Explanation

Metastatic gastric adenocarcinoma to ovary



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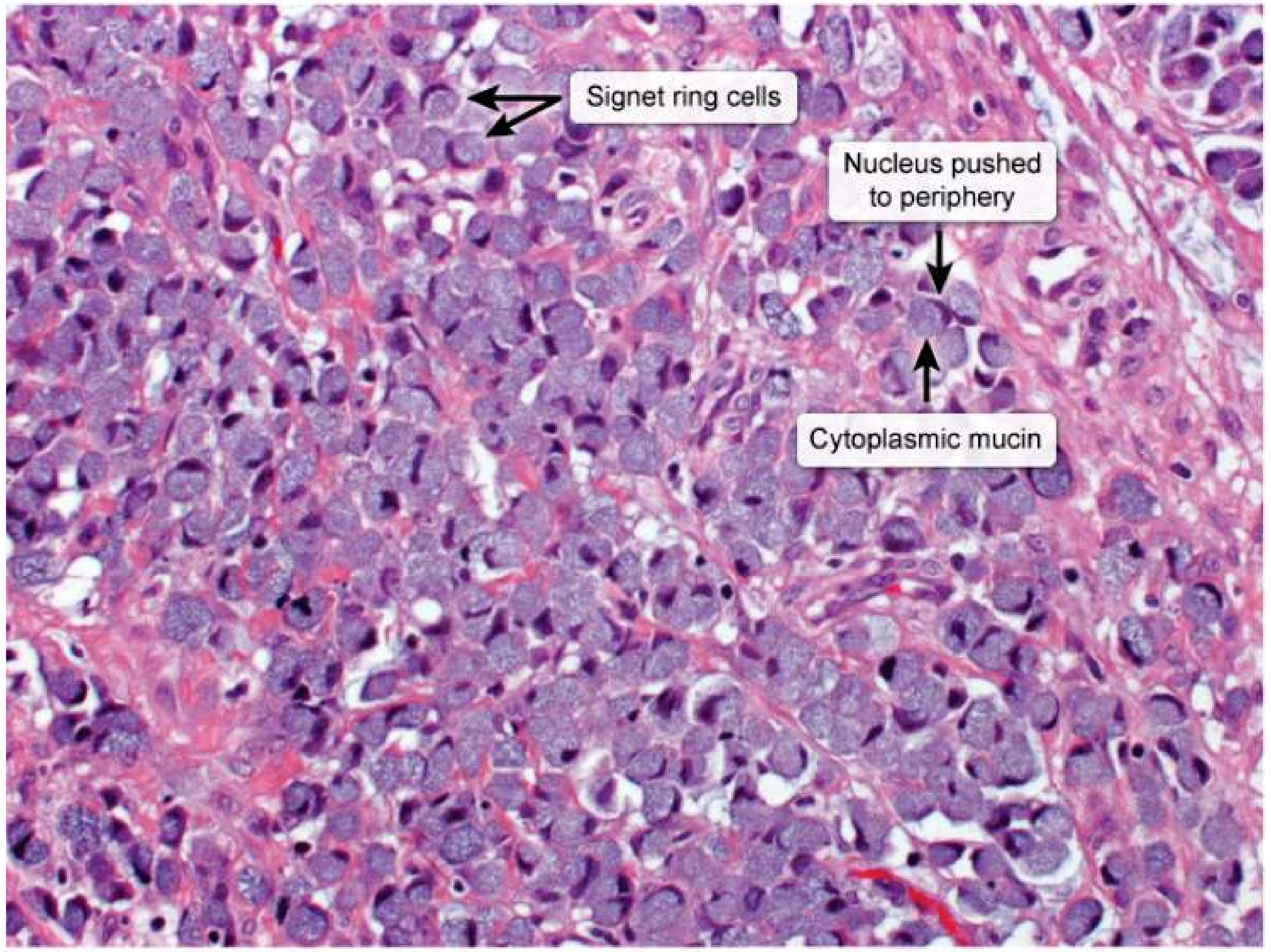
Metastatic gastric adenocarcinoma to ovary



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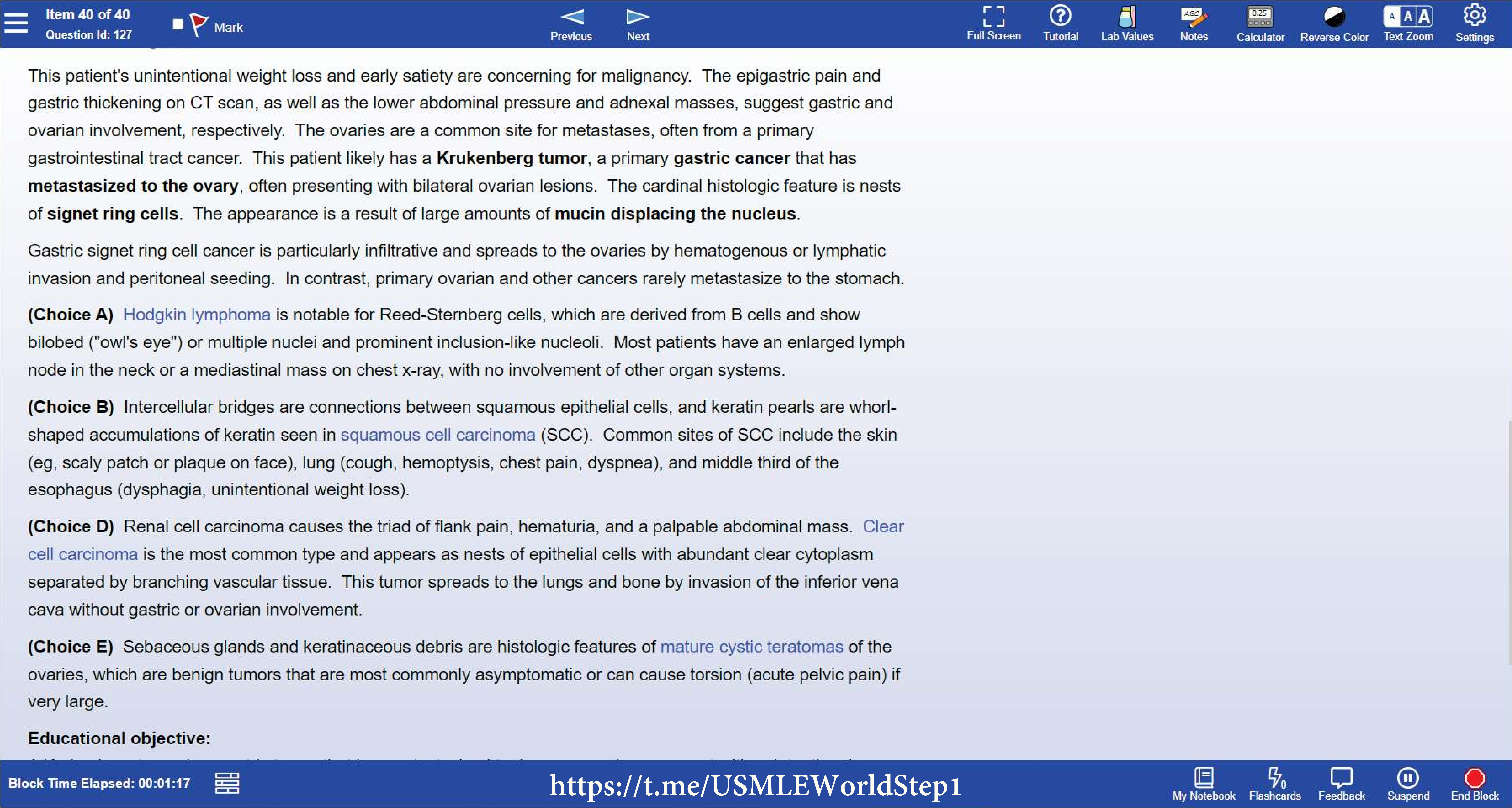
gastrointestinal tract cancer. This patient likely has a **Krukenberg tumor**, a primary **gastric cancer** that has **metastasized to the ovary**, often presenting with bilateral ovarian lesions. The cardinal histologic feature is nests



This patient's unintentional weight loss and early satiety are concerning for malignancy. The epigastric pain and gastric thickening on CT scan, as well as the lower abdominal pressure and adnexal masses, suggest gastric and ovarian involvement, respectively. The ovaries are a common site for metastases, often from a primary gastrointestinal tract cancer. This patient likely has a **Krukenberg tumor**, a primary **gastric cancer** that has **metastasized to the ovary**, often presenting with bilateral ovarian lesions. The cardinal histologic feature is nests of **signet ring cells**. The appearance is a result of large amounts of **mucin displacing the nucleus**.

Gastric signet ring cell cancer is particularly infiltrative and spreads to the ovaries by hematogenous or lymphatic invasion and peritoneal seeding. In contrast, primary ovarian and other cancers rarely metastasize to the stomach.

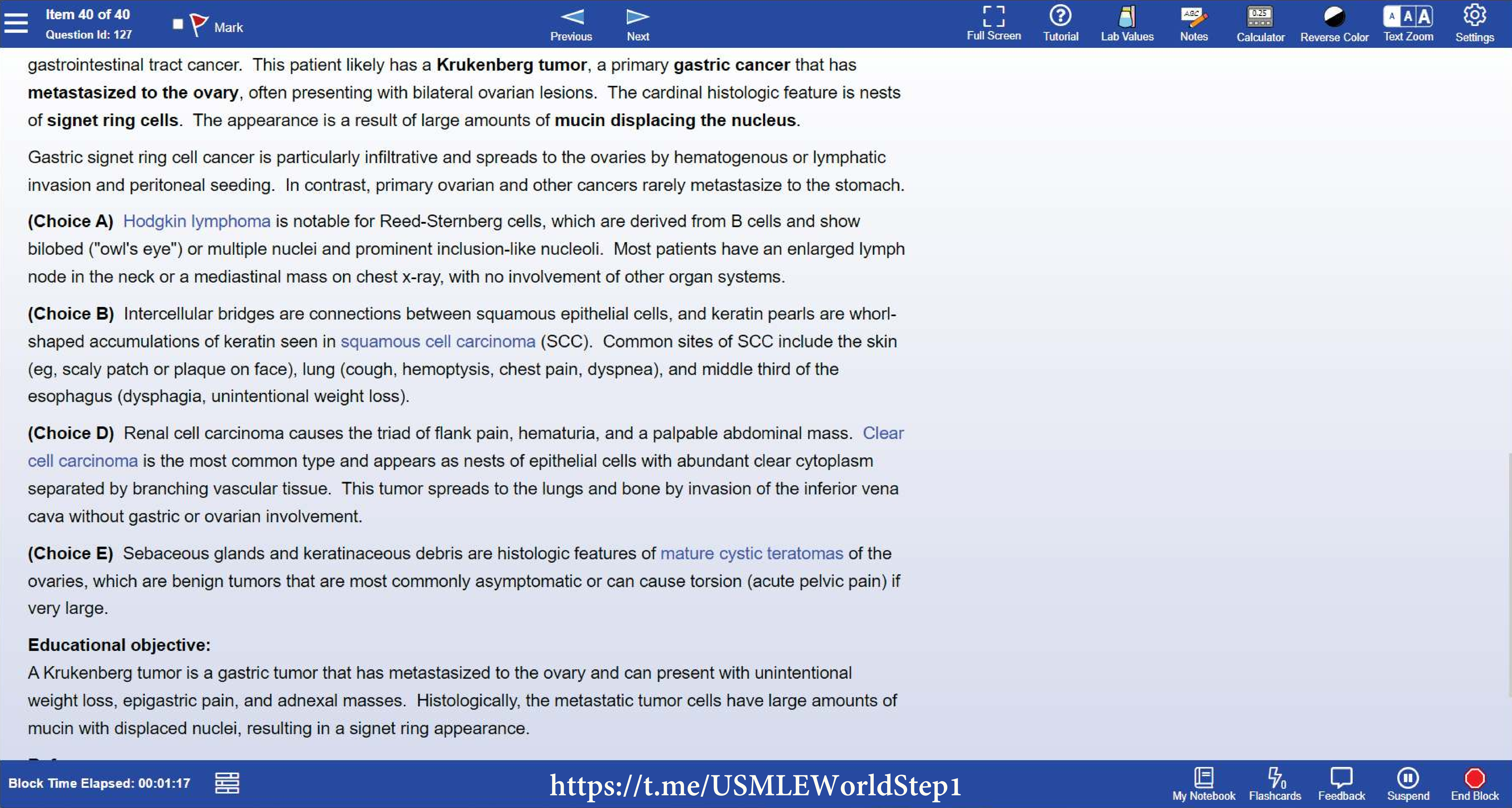
(Choice A) Hodgkin lymphoma is notable for Reed-Sternberg cells, which are derived from B cells and show bilobed ("owl's eye") or multiple nuclei and prominent inclusion-like nucleoli. Most patients have an enlarged lymph node in the neck or a mediastinal mass on chest x-ray, with no involvement of other organ systems.

(Choice B) Intercellular bridges are connections between squamous epithelial cells, and keratin pearls are whorl-shaped accumulations of keratin seen in squamous cell carcinoma (SCC). Common sites of SCC include the skin (eg, scaly patch or plaque on face), lung (cough, hemoptysis, chest pain, dyspnea), and middle third of the esophagus (dysphagia, unintentional weight loss).

(Choice D) Renal cell carcinoma causes the triad of flank pain, hematuria, and a palpable abdominal mass. Clear cell carcinoma is the most common type and appears as nests of epithelial cells with abundant clear cytoplasm separated by branching vascular tissue. This tumor spreads to the lungs and bone by invasion of the inferior vena cava without gastric or ovarian involvement.

(Choice E) Sebaceous glands and keratinaceous debris are histologic features of mature cystic teratomas of the ovaries, which are benign tumors that are most commonly asymptomatic or can cause torsion (acute pelvic pain) if very large.

Educational objective:



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Educational objective:
A Krukenberg tumor is a gastric tumor that has metastasized to the ovary and can present with unintentional weight loss, epigastric pain, and adnexal masses. Histologically, the metastatic tumor cells have large amounts of mucin with displaced nuclei, resulting in a signet ring appearance.

This patient's unintentional weight loss and early satiety are concerning for malignancy. The epigastric pain and

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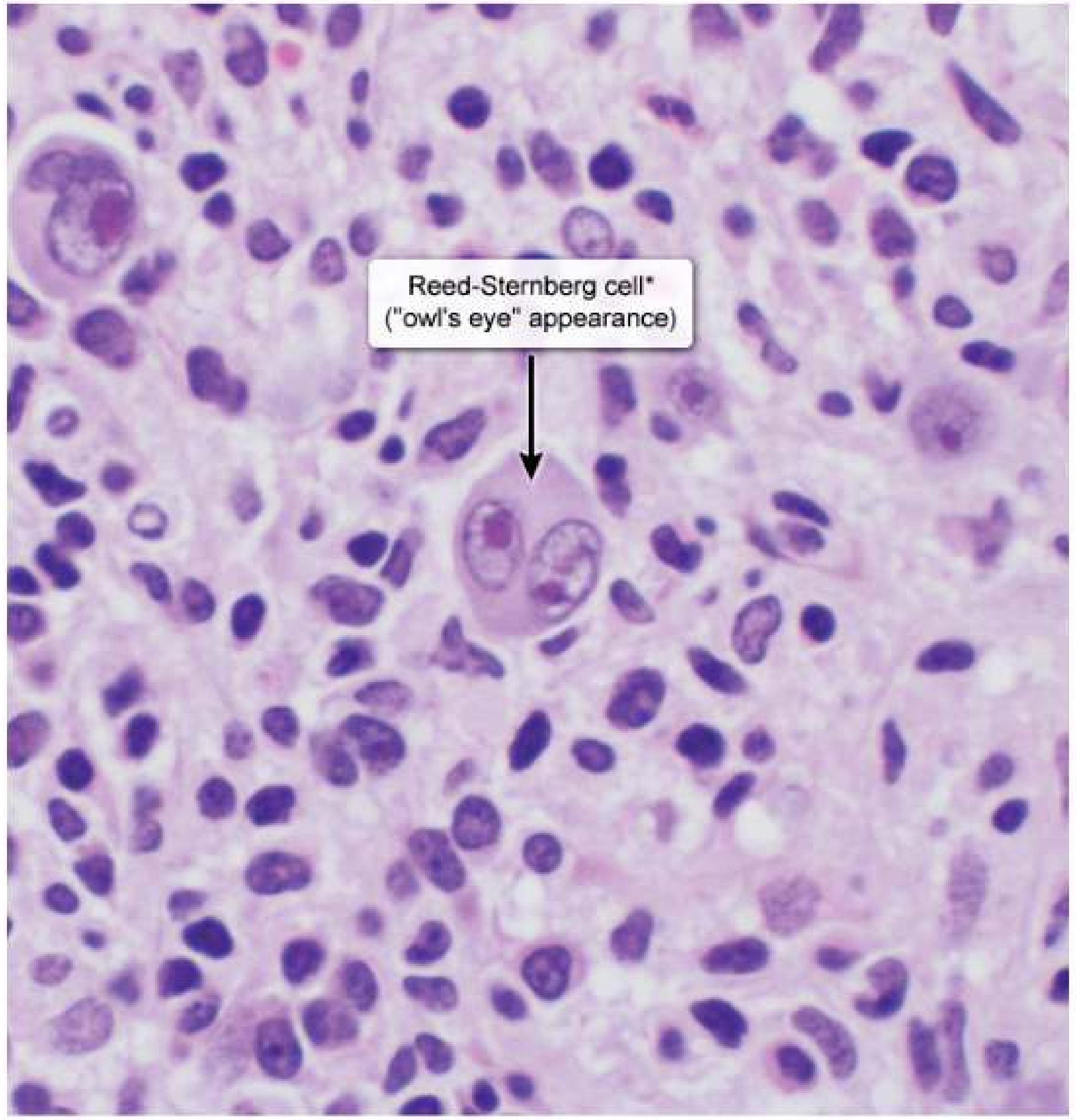
Hodgkin lymphoma



*Large neoplastic cell with lobated nucleus or multiple nuclei and prominent nucleoli

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Educational objective:

A Krukenberg tumor is a gastric tumor that has metastasized to the ovary and can present with unintentional

This patient's unintentional weight loss and early satiety are concerning for malignancy. The epigastric pain and

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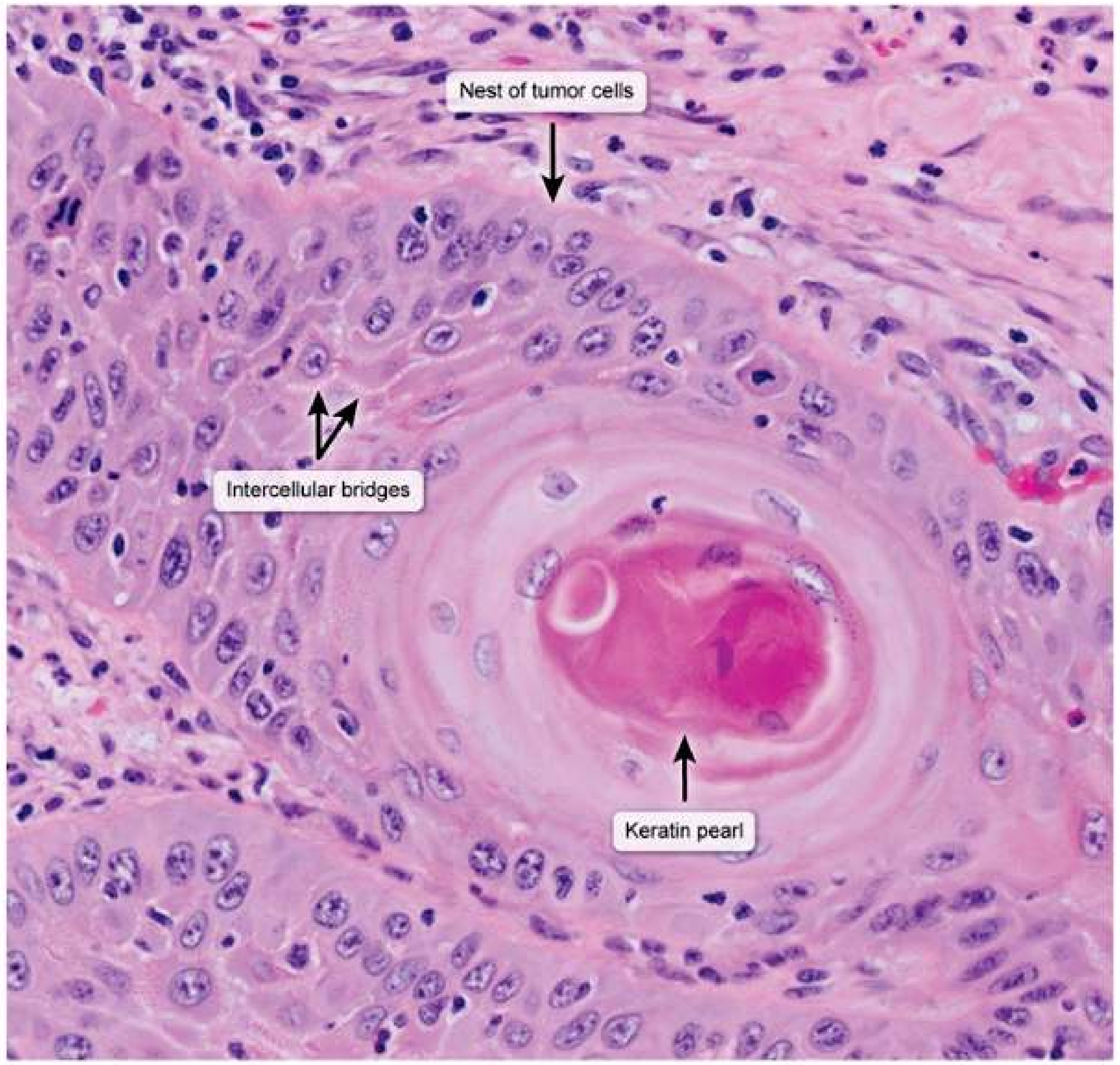
Squamous cell carcinoma



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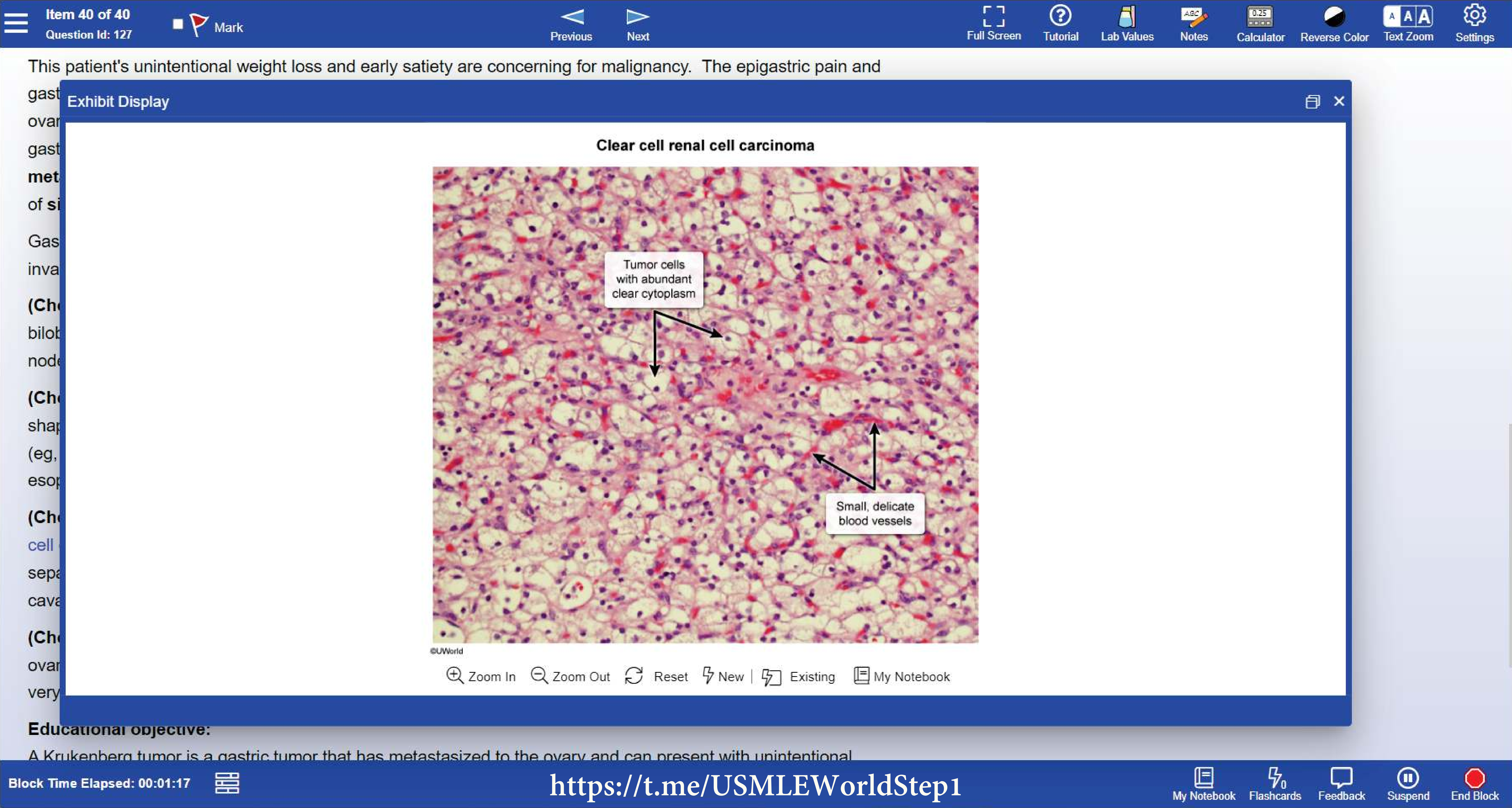
Educational objective:

A Krukenberg tumor is a gastric tumor that has metastasized to the ovary and can present with unintentional



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Clear cell renal cell carcinoma

Tumor cells with abundant clear cytoplasm
Small, delicate blood vessels
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Educational objective:

A Krukenberg tumor is a gastric tumor that has metastasized to the ovary and can present with unintentional

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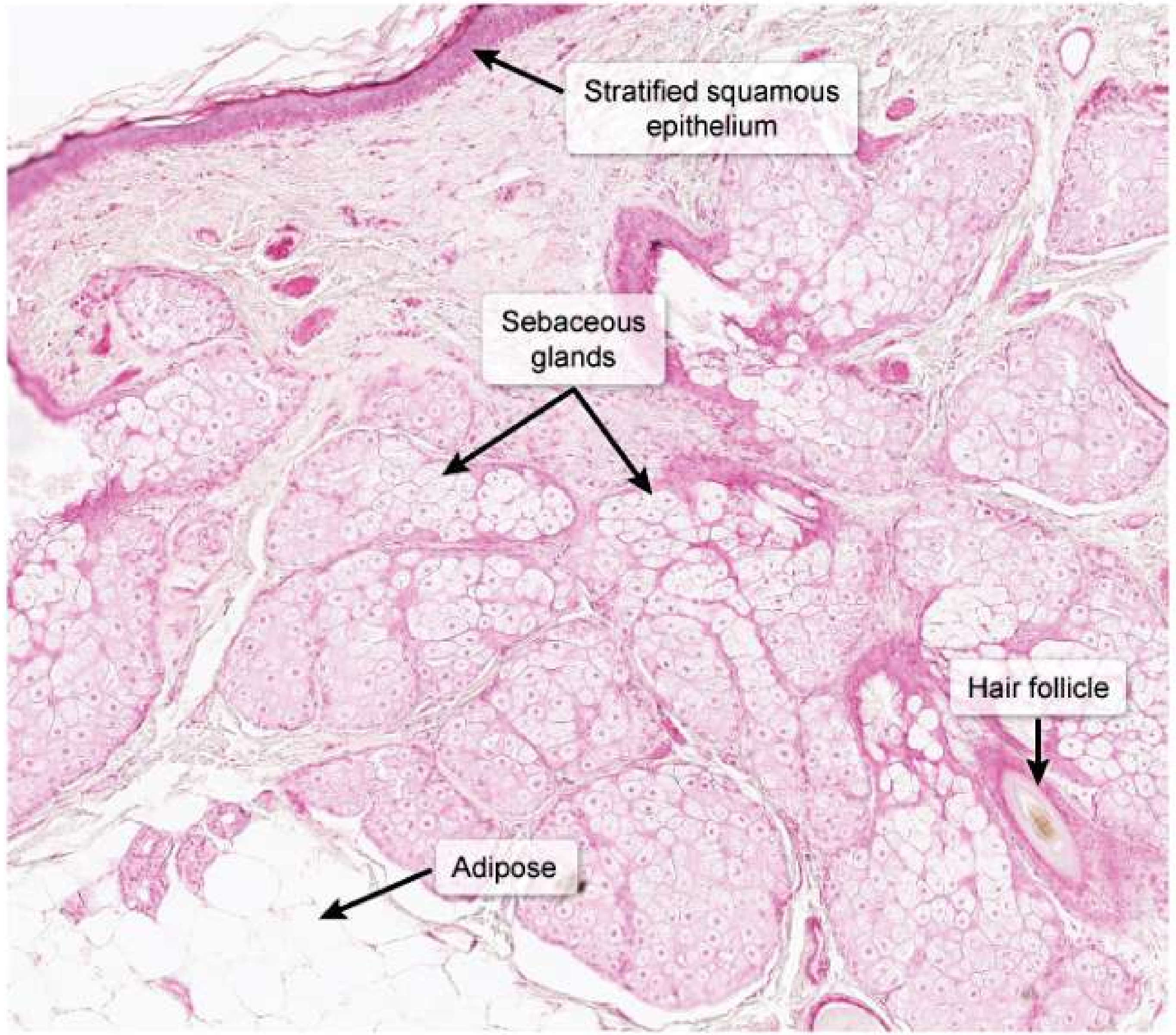
Ovarian mature teratoma


Stratified squamous epithelium
Sebaceous glands
Hair follicle
Adipose

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Educational objective:

A Krukenberg tumor is a gastric tumor that has metastasized to the ovary and can present with unintentional

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A 32-year-old woman, gravida 4 para 0, comes to the office for evaluation of recurrent pregnancy loss. She has had 4 consecutive spontaneous abortions with the same partner. The patient has menstrual cycles approximately 28 days apart, with light bleeding for 2-3 days. She has no chronic medical conditions and takes no daily medications. The patient does not use tobacco, alcohol, or illicit drugs. Results of her hysterosalpingogram are shown in the exhibit. Failure of which of the following processes is the most likely underlying mechanism of this patient's condition?

- ○ A. Development of the paramesonephric ducts
- ○ B. Differentiation of the mesonephric tubules
- ○ C. Fusion of the mesonephric ducts
- ○ D. Lateral fusion of the paramesonephric ducts
- ○ E. Vertical fusion of the paramesonephric ducts with the urogenital sinus

A 32-year-old woman, gravida 4 para 0, comes to the office for evaluation of recurrent pregnancy loss. She has

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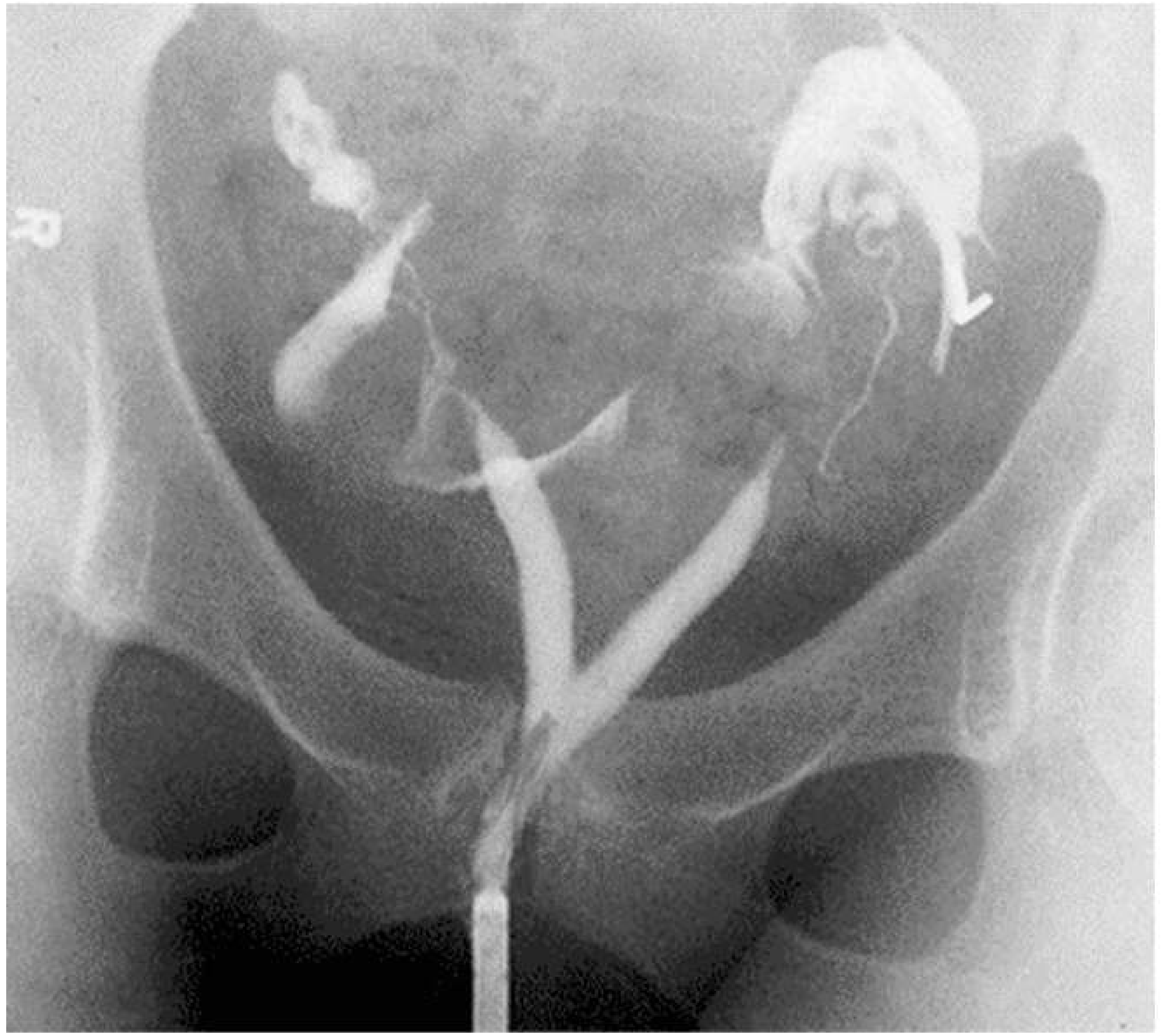

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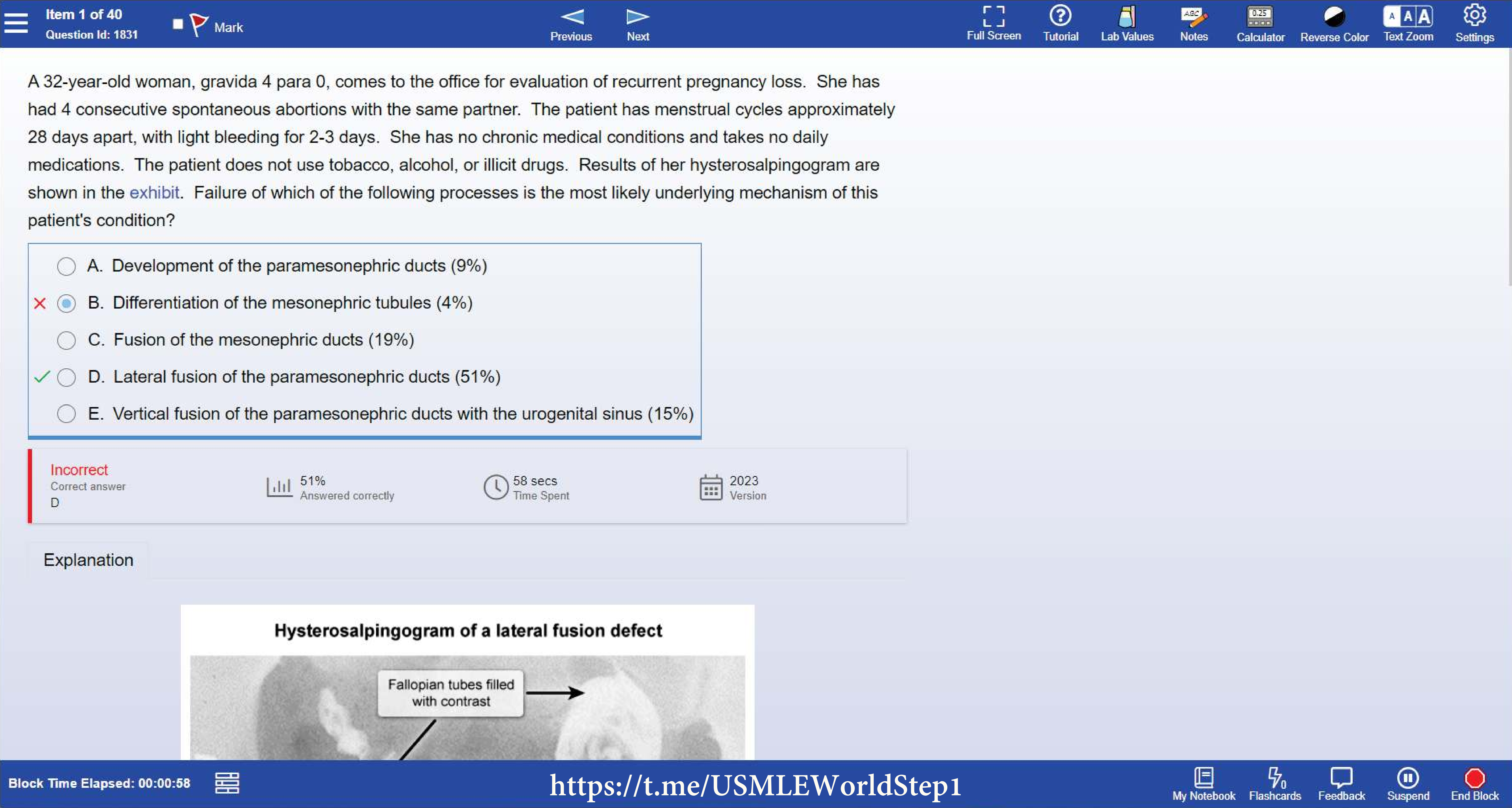
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- ○ A. Development of the paramesonephric ducts (9%)
- ✗ ● B. Differentiation of the mesonephric tubules (4%)
- ○ C. Fusion of the mesonephric ducts (19%)
- ✓ ○ D. Lateral fusion of the paramesonephric ducts (51%)
- ○ E. Vertical fusion of the paramesonephric ducts with the urogenital sinus (15%)

Incorrect
Correct answer
D

51%
Answered correctly

58 secs
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Explanation

Hysterosalpingogram of a lateral fusion defect

Fallopian tubes filled with contrast
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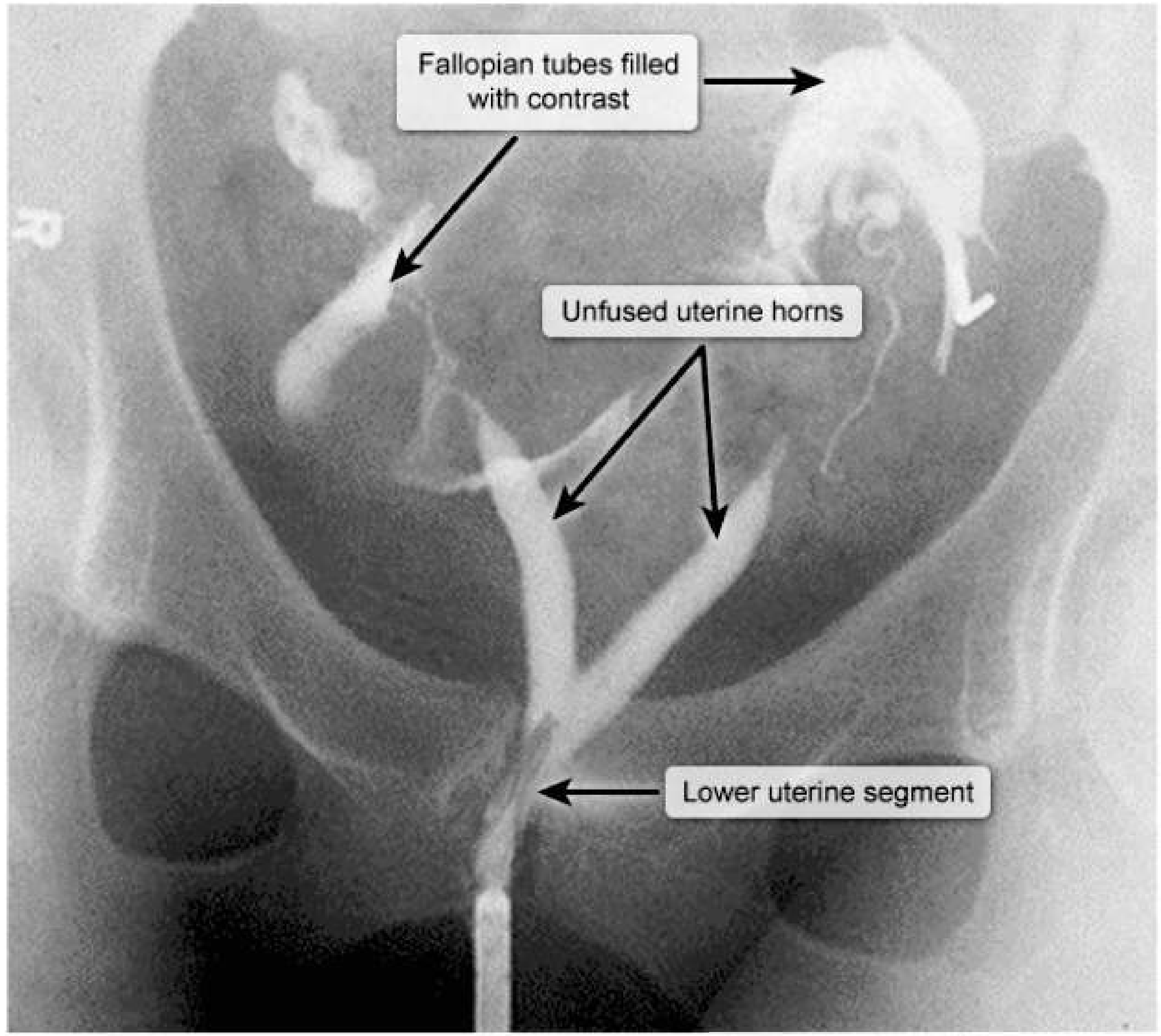
Explanation

Exhibit Display

Hysterosalpingogram of a lateral fusion defect


Fallopian tubes filled with contrast
R
Unfused uterine horns
Lower uterine segment

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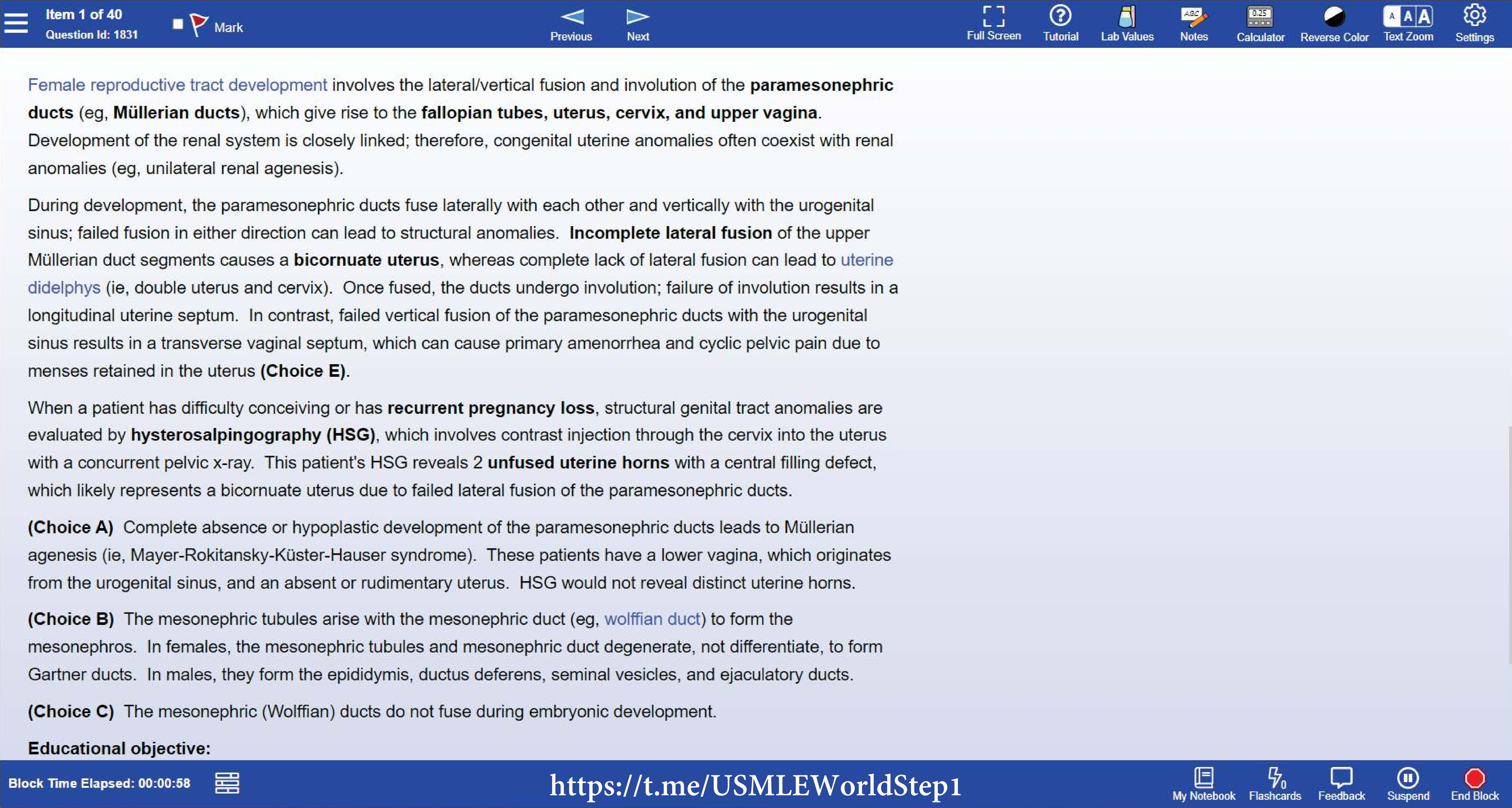
Female reproductive tract development involves the lateral/vertical fusion and involution of the **paramesonephric ducts** (eg, **Müllerian ducts**), which give rise to the **fallopian tubes, uterus, cervix, and upper vagina**.



Female reproductive tract development involves the lateral/vertical fusion and involution of the **paramesonephric ducts** (eg, **Müllerian ducts**), which give rise to the **fallopian tubes, uterus, cervix, and upper vagina**. Development of the renal system is closely linked; therefore, congenital uterine anomalies often coexist with renal anomalies (eg, unilateral renal agenesis).

During development, the paramesonephric ducts fuse laterally with each other and vertically with the urogenital sinus; failed fusion in either direction can lead to structural anomalies. **Incomplete lateral fusion** of the upper Müllerian duct segments causes a **bicornuate uterus**, whereas complete lack of lateral fusion can lead to uterine didelphys (ie, double uterus and cervix). Once fused, the ducts undergo involution; failure of involution results in a longitudinal uterine septum. In contrast, failed vertical fusion of the paramesonephric ducts with the urogenital sinus results in a transverse vaginal septum, which can cause primary amenorrhea and cyclic pelvic pain due to menses retained in the uterus **(Choice E)**.

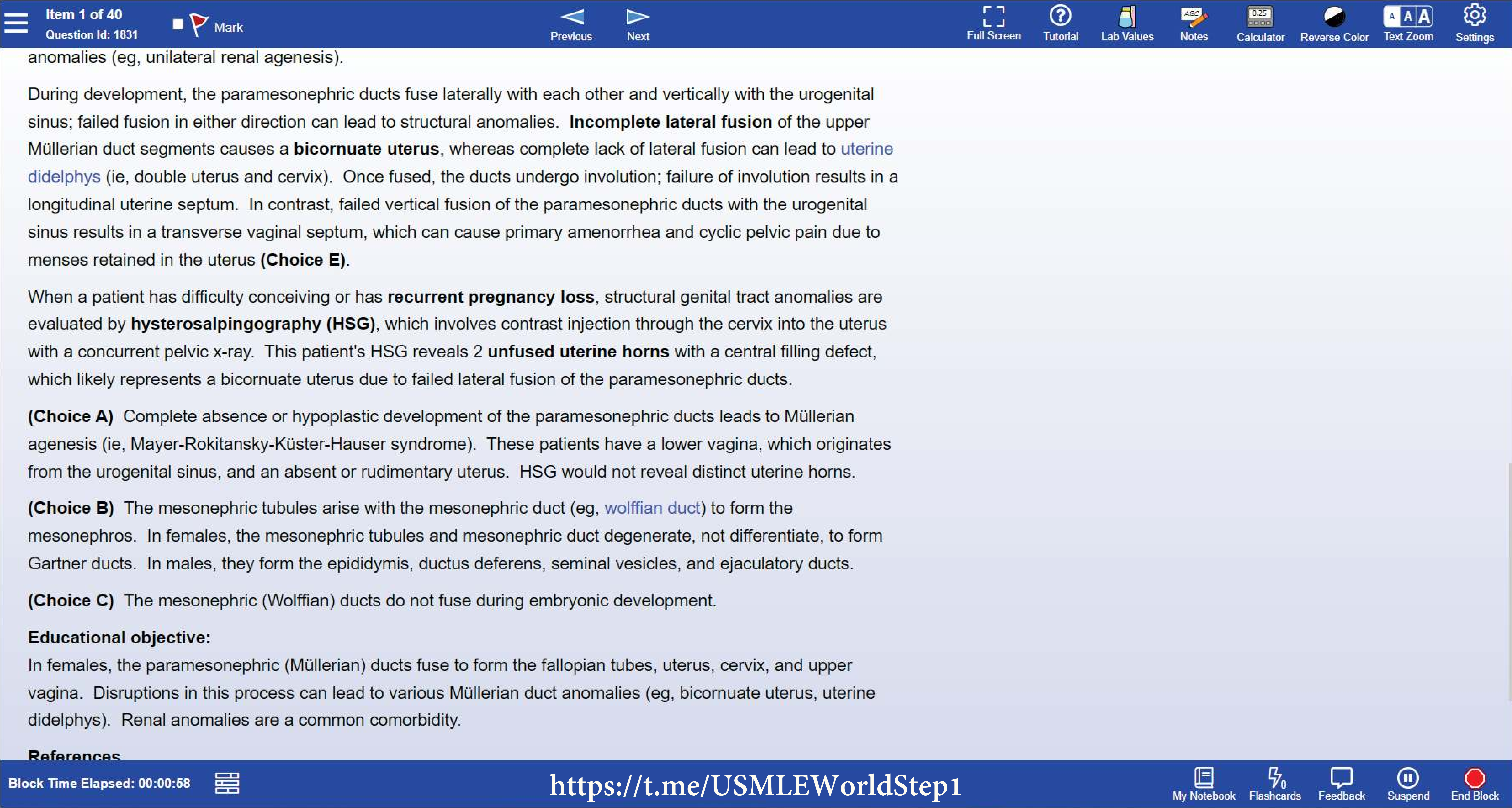
When a patient has difficulty conceiving or has **recurrent pregnancy loss**, structural genital tract anomalies are evaluated by **hysterosalpingography (HSG)**, which involves contrast injection through the cervix into the uterus with a concurrent pelvic x-ray. This patient's HSG reveals 2 **unfused uterine horns** with a central filling defect, which likely represents a bicornuate uterus due to failed lateral fusion of the paramesonephric ducts.

(Choice A) Complete absence or hypoplastic development of the paramesonephric ducts leads to Müllerian agenesis (ie, Mayer-Rokitansky-Küster-Hauser syndrome). These patients have a lower vagina, which originates from the urogenital sinus, and an absent or rudimentary uterus. HSG would not reveal distinct uterine horns.

(Choice B) The mesonephric tubules arise with the mesonephric duct (eg, wolffian duct) to form the mesonephros. In females, the mesonephric tubules and mesonephric duct degenerate, not differentiate, to form Gartner ducts. In males, they form the epididymis, ductus deferens, seminal vesicles, and ejaculatory ducts.

(Choice C) The mesonephric (Wolffian) ducts do not fuse during embryonic development.

Educational objective:



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(Choice C) The mesonephric (Wolffian) ducts do not fuse during embryonic development.

Educational objective:

In females, the paramesonephric (Müllerian) ducts fuse to form the fallopian tubes, uterus, cervix, and upper vagina. Disruptions in this process can lead to various Müllerian duct anomalies (eg, bicornuate uterus, uterine didelphys). Renal anomalies are a common comorbidity.

References

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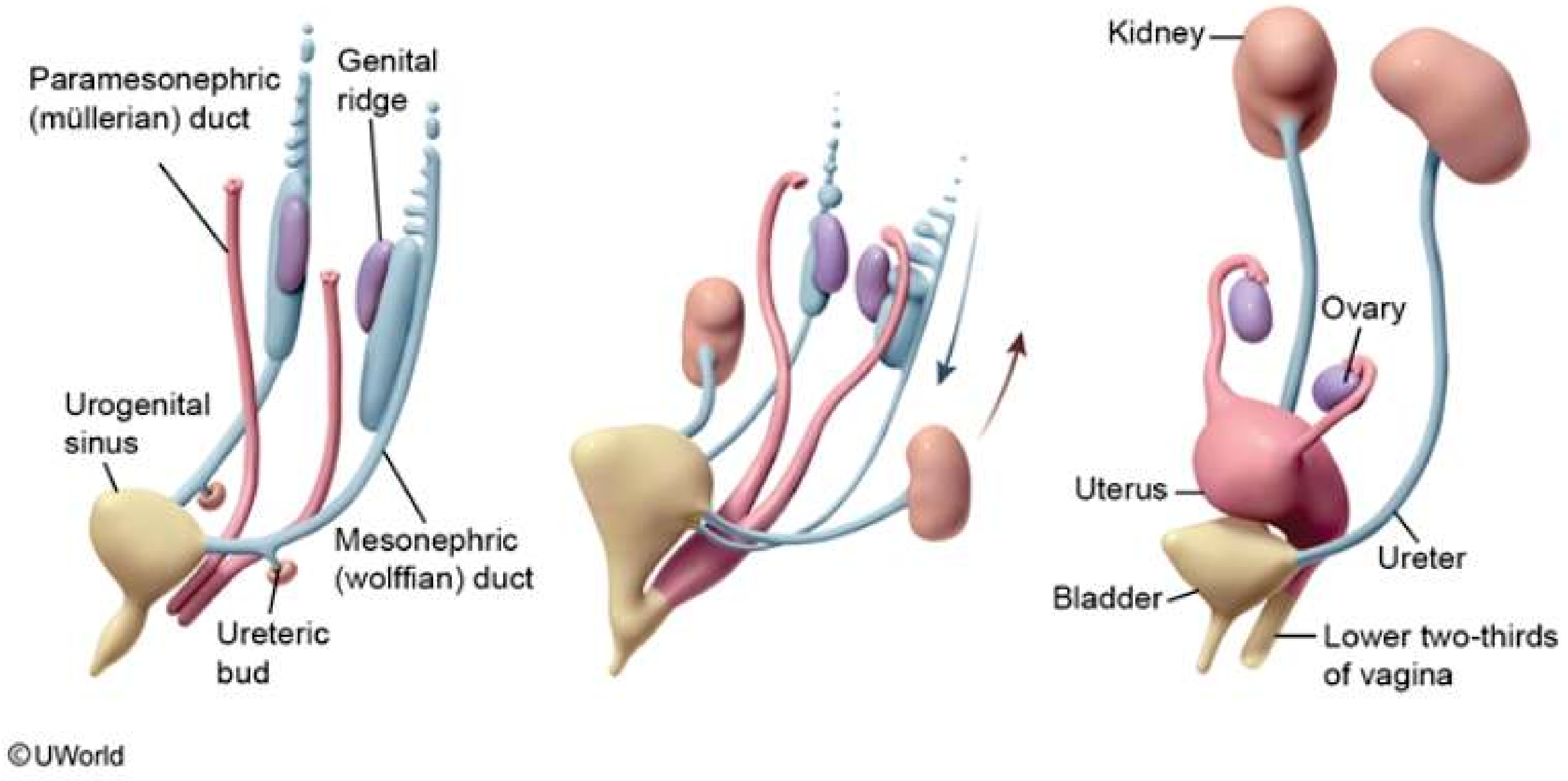
Urogenital development


Paramesonephric (müllerian) duct
Genital ridge
Urogenital sinus
Mesonephric (wolffian) duct
Ureteric bud
Kidney
Ovary
Uterus
Ureter
Bladder
Lower two-thirds of vagina

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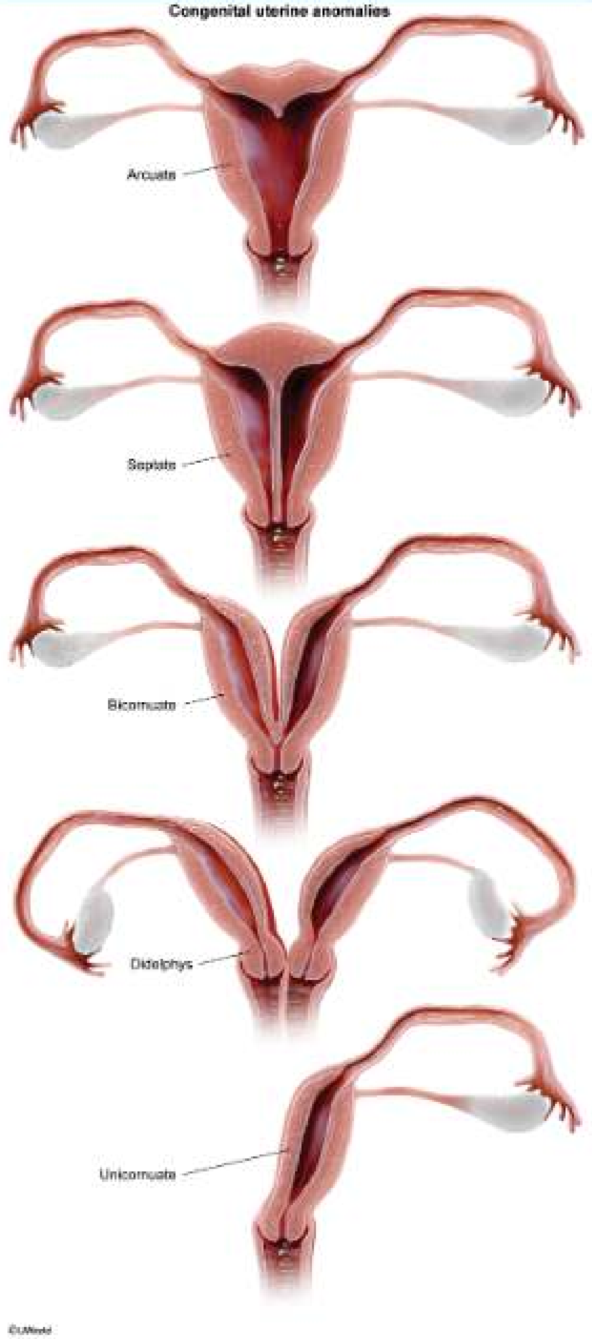
Congenital uterine anomalies
Arcuate
Septate
Bicornuate
Didelphys
Unicornuate
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(Choice B) The mesonephric tubules arise with the mesonephric duct (eg, wolffian duct) to form the anomalies (eg, unilateral renal agenesis).

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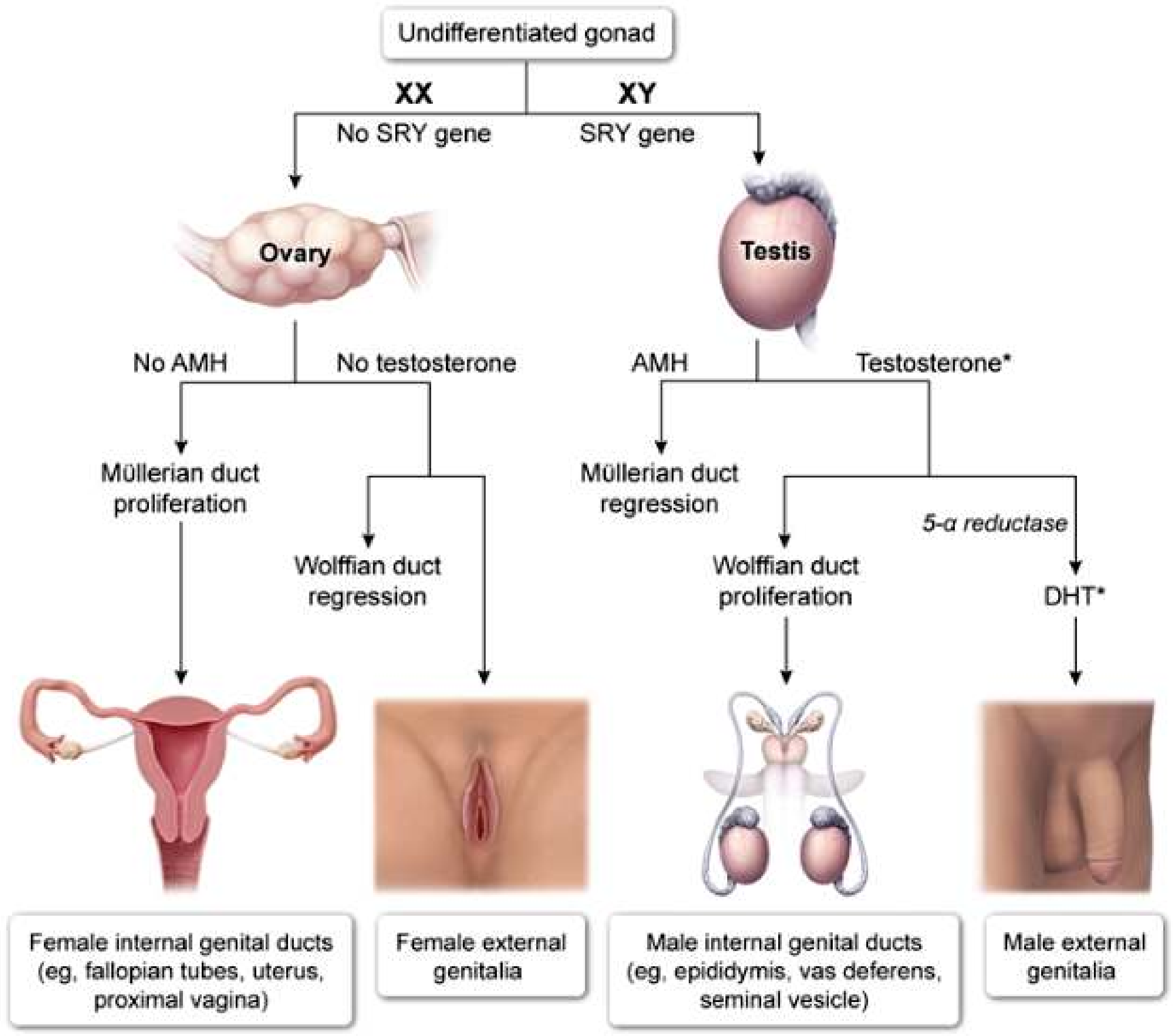
Fetal sex differentiation


Undifferentiated gonad
XX
No SRY gene
XY
SRY gene
Ovary
Testis
No AMH
No testosterone
AMH
Testosterone*
Müllerian duct proliferation
Wolffian duct regression
Müllerian duct regression
5-α reductase
Wolffian duct proliferation
DHT*
Female internal genital ducts (eg, fallopian tubes, uterus, proximal vagina)
Female external genitalia
Male internal genital ducts (eg, epididymis, vas deferens, seminal vesicle)
Male external genitalia

*Via action on androgen receptor.
AMH = antimüllerian hormone; **DHT** = dihydrotestosterone.

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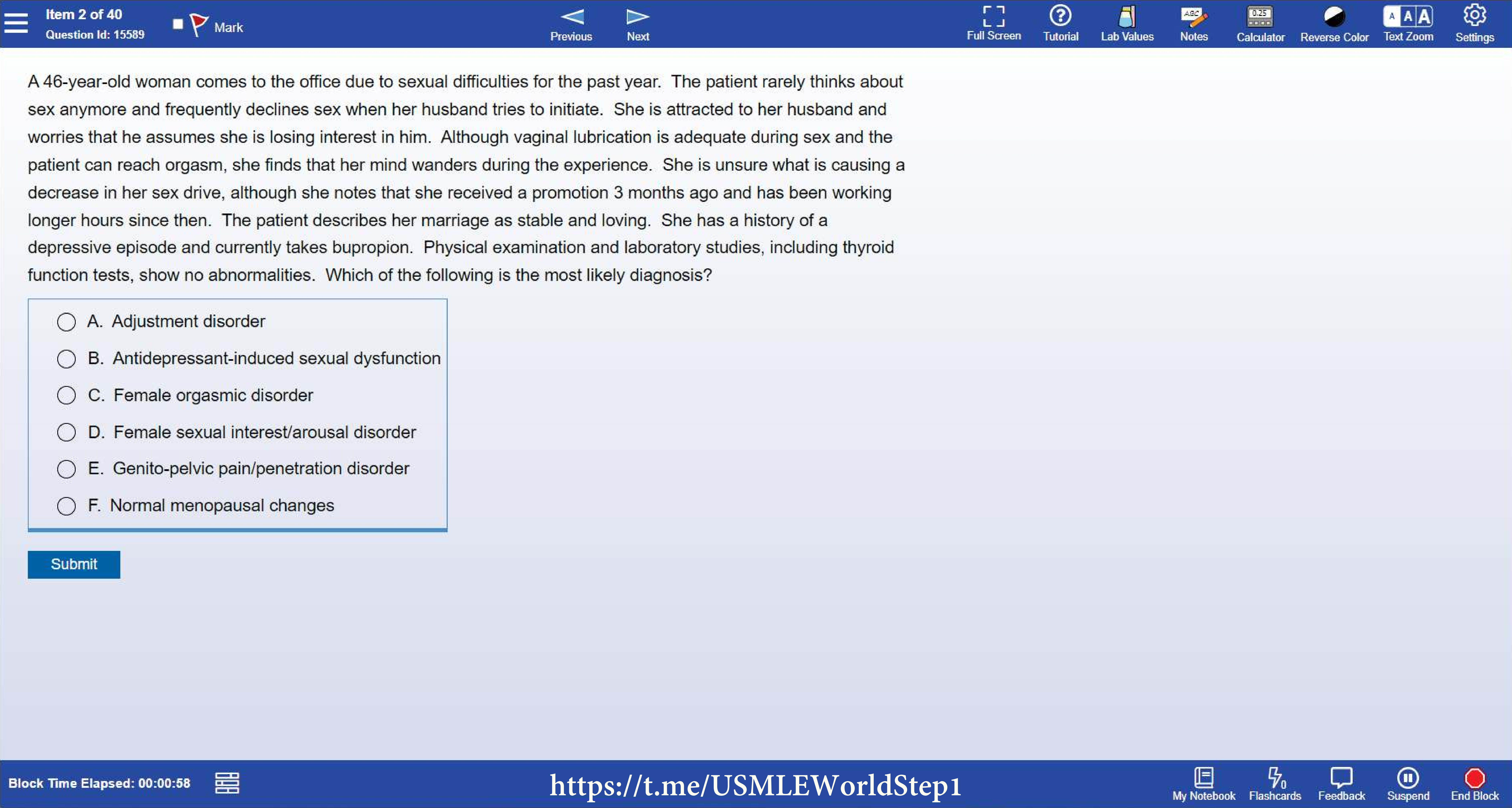
References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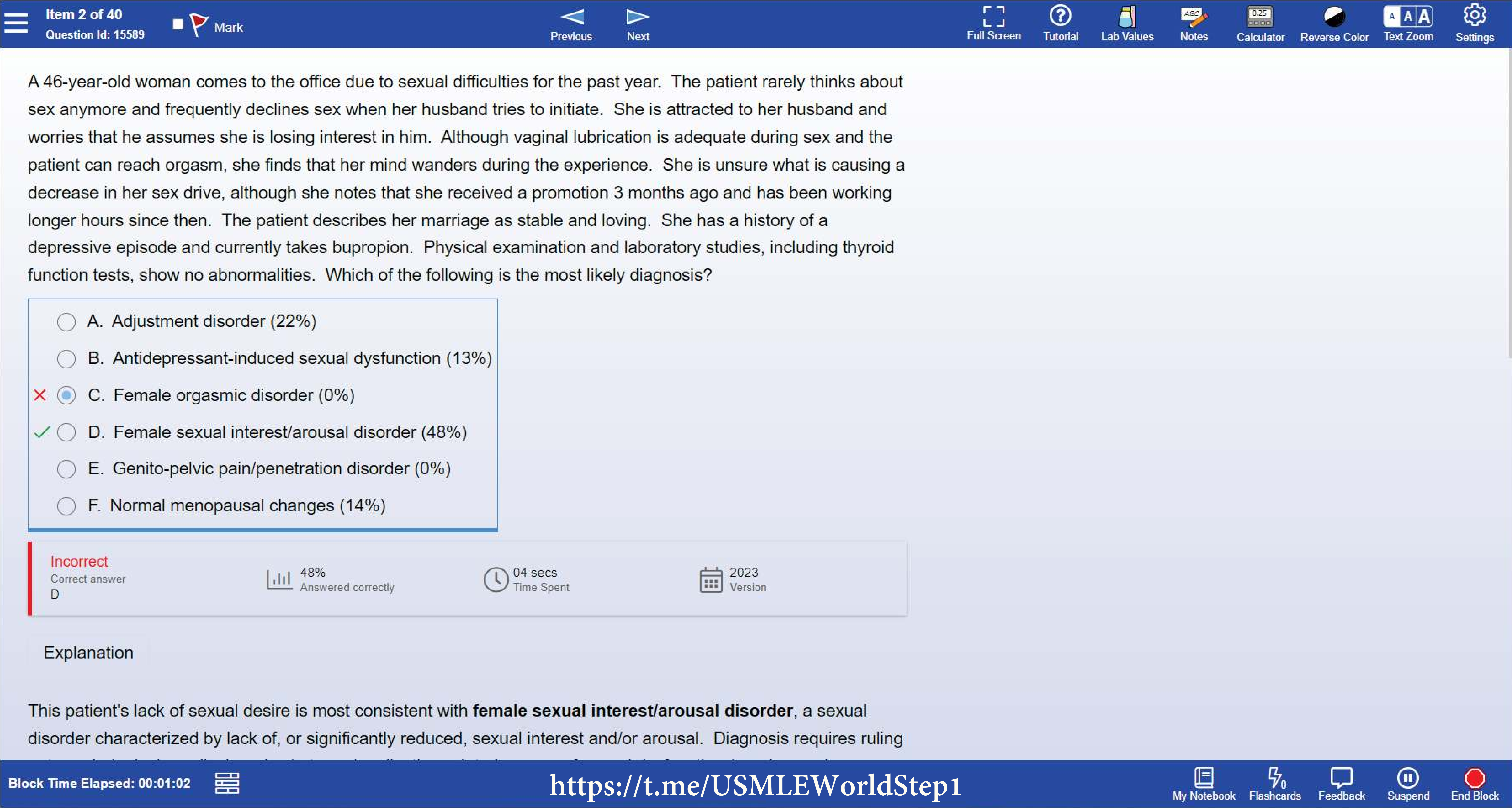
A 46-year-old woman comes to the office due to sexual difficulties for the past year. The patient rarely thinks about sex anymore and frequently declines sex when her husband tries to initiate. She is attracted to her husband and worries that he assumes she is losing interest in him. Although vaginal lubrication is adequate during sex and the patient can reach orgasm, she finds that her mind wanders during the experience. She is unsure what is causing a decrease in her sex drive, although she notes that she received a promotion 3 months ago and has been working longer hours since then. The patient describes her marriage as stable and loving. She has a history of a depressive episode and currently takes bupropion. Physical examination and laboratory studies, including thyroid function tests, show no abnormalities. Which of the following is the most likely diagnosis?

○ A. Adjustment disorder
○ B. Antidepressant-induced sexual dysfunction
○ C. Female orgasmic disorder
○ D. Female sexual interest/arousal disorder
○ E. Genito-pelvic pain/penetration disorder
○ F. Normal menopausal changes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- ○ A. Adjustment disorder (22%)
- ○ B. Antidepressant-induced sexual dysfunction (13%)
- ✗ ● C. Female orgasmic disorder (0%)
- ✓ ○ D. Female sexual interest/arousal disorder (48%)
- ○ E. Genito-pelvic pain/penetration disorder (0%)
- ○ F. Normal menopausal changes (14%)

Incorrect
Correct answer
D

48%
Answered correctly

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Explanation

This patient's lack of sexual desire is most consistent with **female sexual interest/arousal disorder**, a sexual disorder characterized by lack of, or significantly reduced, sexual interest and/or arousal. Diagnosis requires ruling

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This patient's lack of sexual desire is most consistent with **female sexual interest/arousal disorder**, a sexual disorder characterized by lack of, or significantly reduced, sexual interest and/or arousal. Diagnosis requires ruling out psychological, medical, and substance/medication-related causes of sexual dysfunction (eg, depression, diabetes, chronic alcohol or drug use) and relationship problems.

The diagnosis of female sexual interest/arousal disorder encompasses symptoms of **decreased interest, decreased arousal, or both**. This patient primarily experiences decreased interest (ie, lack of sexual thoughts; reduced initiation of sexual activity or receptivity to a partner's attempts to initiate, but adequate lubrication/orgasm). Symptoms related to arousal may include decreased excitement/pleasure in response to mental and physical sexual cues and encounters.

(Choice A) Although the patient mentions that her condition is worse since her promotion 3 months ago, there is evidence of a change in sexual functioning preceding this stressful event.

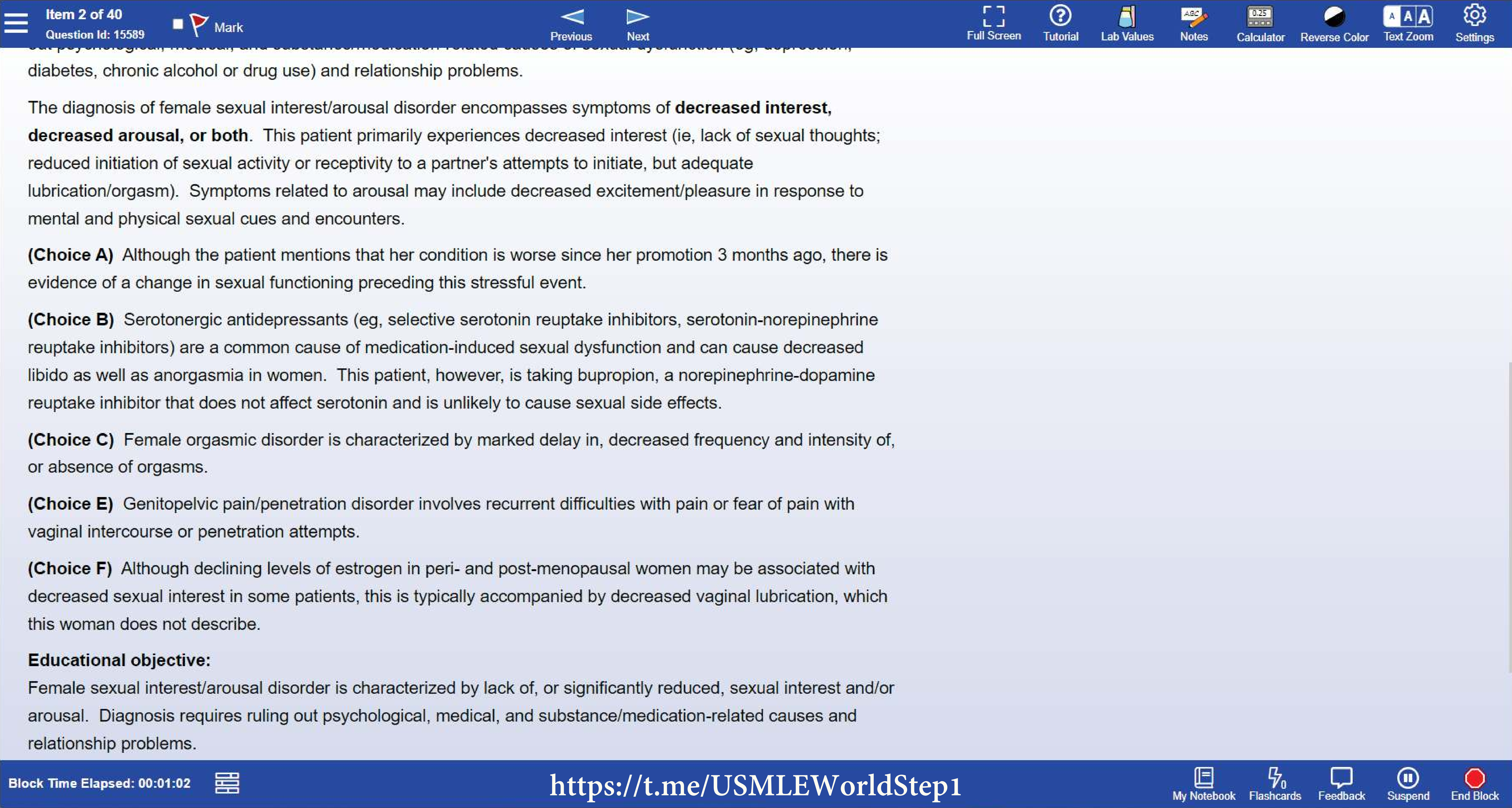
(Choice B) Serotonergic antidepressants (eg, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors) are a common cause of medication-induced sexual dysfunction and can cause decreased libido as well as anorgasmia in women. This patient, however, is taking bupropion, a norepinephrine-dopamine reuptake inhibitor that does not affect serotonin and is unlikely to cause sexual side effects.

(Choice C) Female orgasmic disorder is characterized by marked delay in, decreased frequency and intensity of, or absence of orgasms.

(Choice E) Genitopelvic pain/penetration disorder involves recurrent difficulties with pain or fear of pain with vaginal intercourse or penetration attempts.

(Choice F) Although declining levels of estrogen in peri- and post-menopausal women may be associated with decreased sexual interest in some patients, this is typically accompanied by decreased vaginal lubrication, which this woman does not describe.

Educational objective:



diabetes, chronic alcohol or drug use) and relationship problems.

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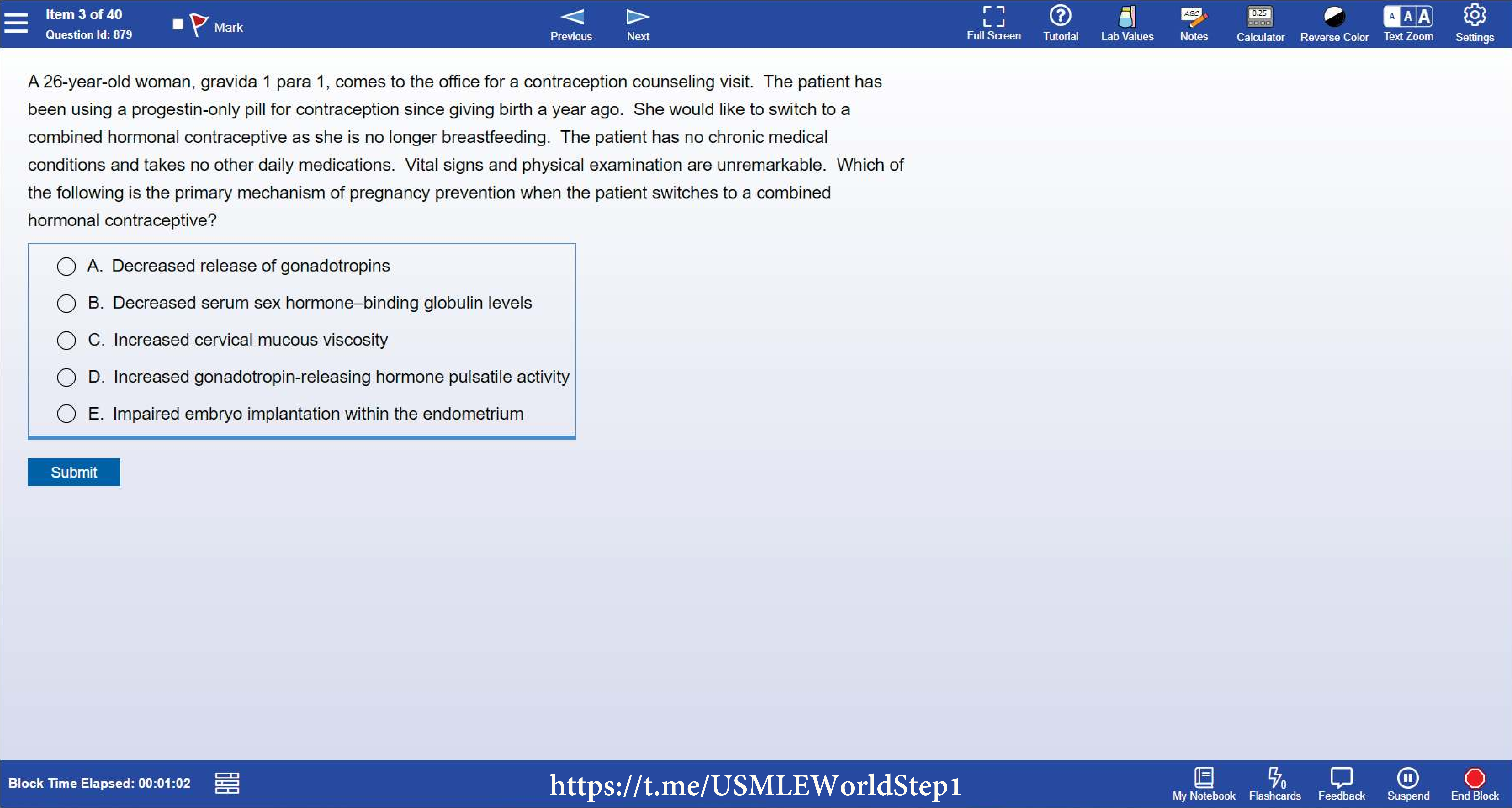
(Choice F) Although declining levels of estrogen in peri- and post-menopausal women may be associated with decreased sexual interest in some patients, this is typically accompanied by decreased vaginal lubrication, which this woman does not describe.

Educational objective:
Female sexual interest/arousal disorder is characterized by lack of, or significantly reduced, sexual interest and/or arousal. Diagnosis requires ruling out psychological, medical, and substance/medication-related causes and relationship problems.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A 26-year-old woman, gravida 1 para 1, comes to the office for a contraception counseling visit. The patient has been using a progestin-only pill for contraception since giving birth a year ago. She would like to switch to a combined hormonal contraceptive as she is no longer breastfeeding. The patient has no chronic medical conditions and takes no other daily medications. Vital signs and physical examination are unremarkable. Which of the following is the primary mechanism of pregnancy prevention when the patient switches to a combined hormonal contraceptive?

- ○ A. Decreased release of gonadotropins
- ○ B. Decreased serum sex hormone–binding globulin levels
- ○ C. Increased cervical mucous viscosity
- ○ D. Increased gonadotropin-releasing hormone pulsatile activity
- ○ E. Impaired embryo implantation within the endometrium

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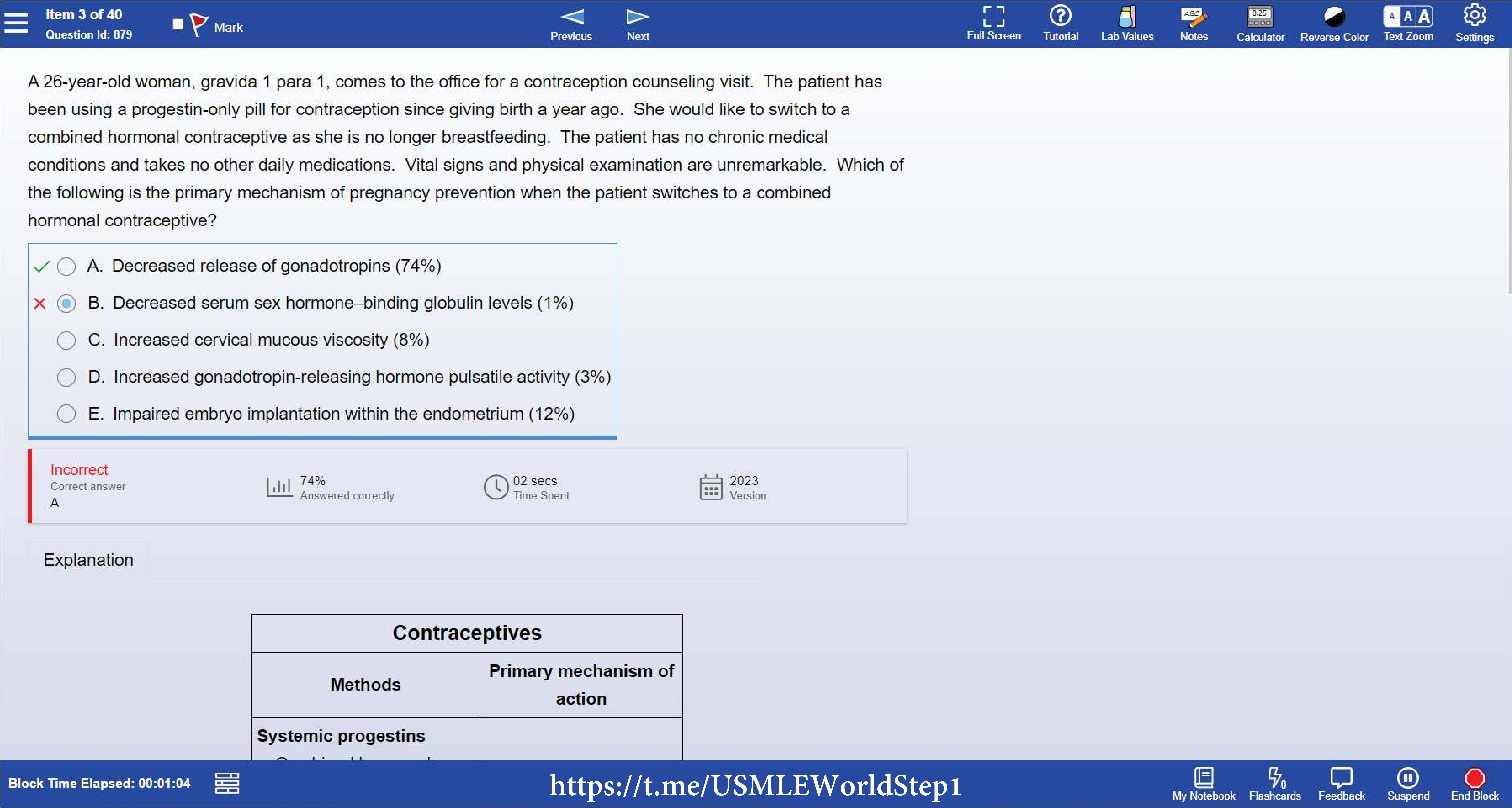
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- ✓ ○ A. Decreased release of gonadotropins (74%)
- ✗ ● B. Decreased serum sex hormone–binding globulin levels (1%)
- ○ C. Increased cervical mucous viscosity (8%)
- ○ D. Increased gonadotropin-releasing hormone pulsatile activity (3%)
- ○ E. Impaired embryo implantation within the endometrium (12%)

Incorrect
Correct answer
A

74%
Answered correctly

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Explanation

Contraceptives	
Methods	**Primary mechanism of action**
Systemic progestins	

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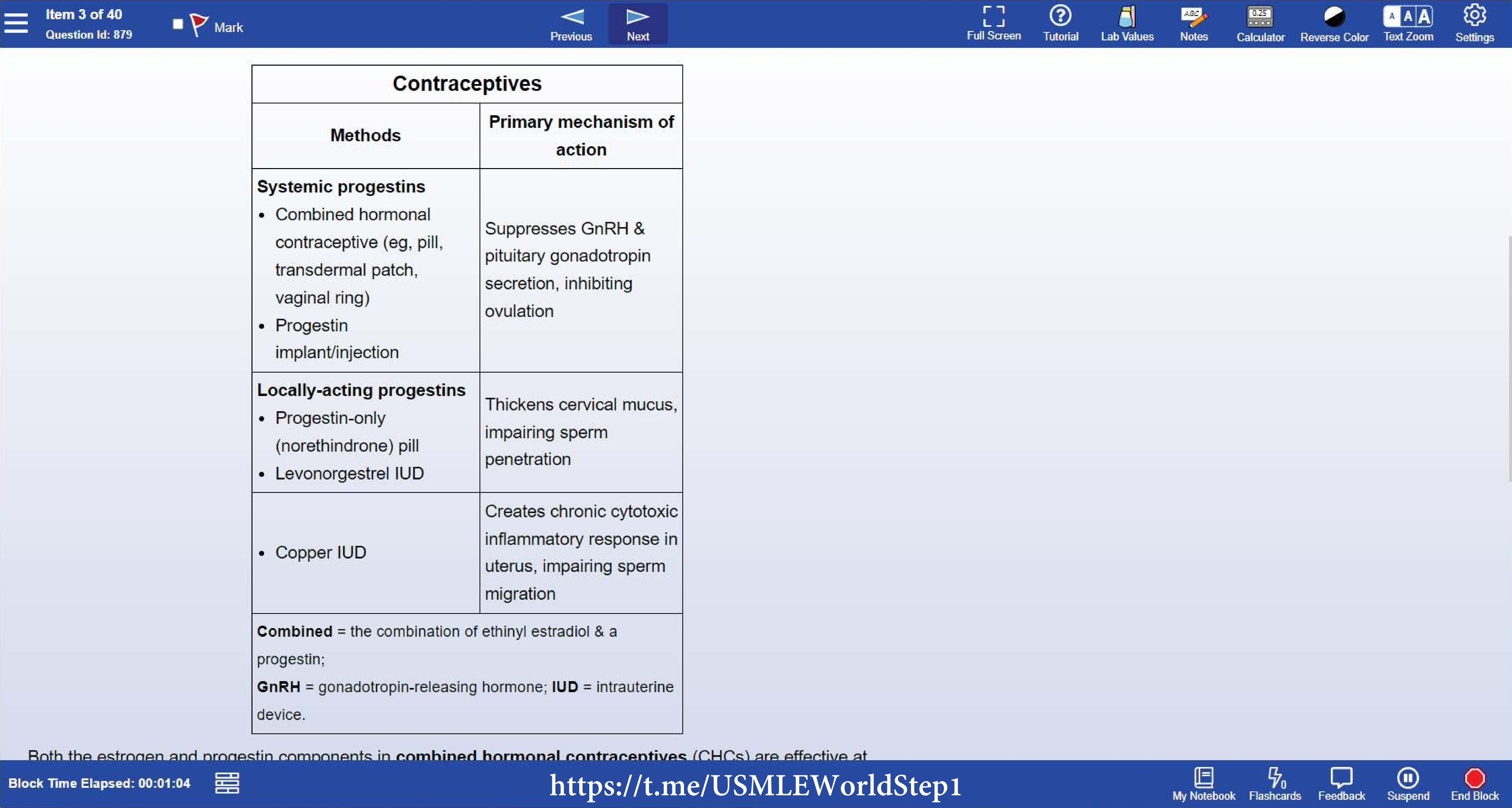
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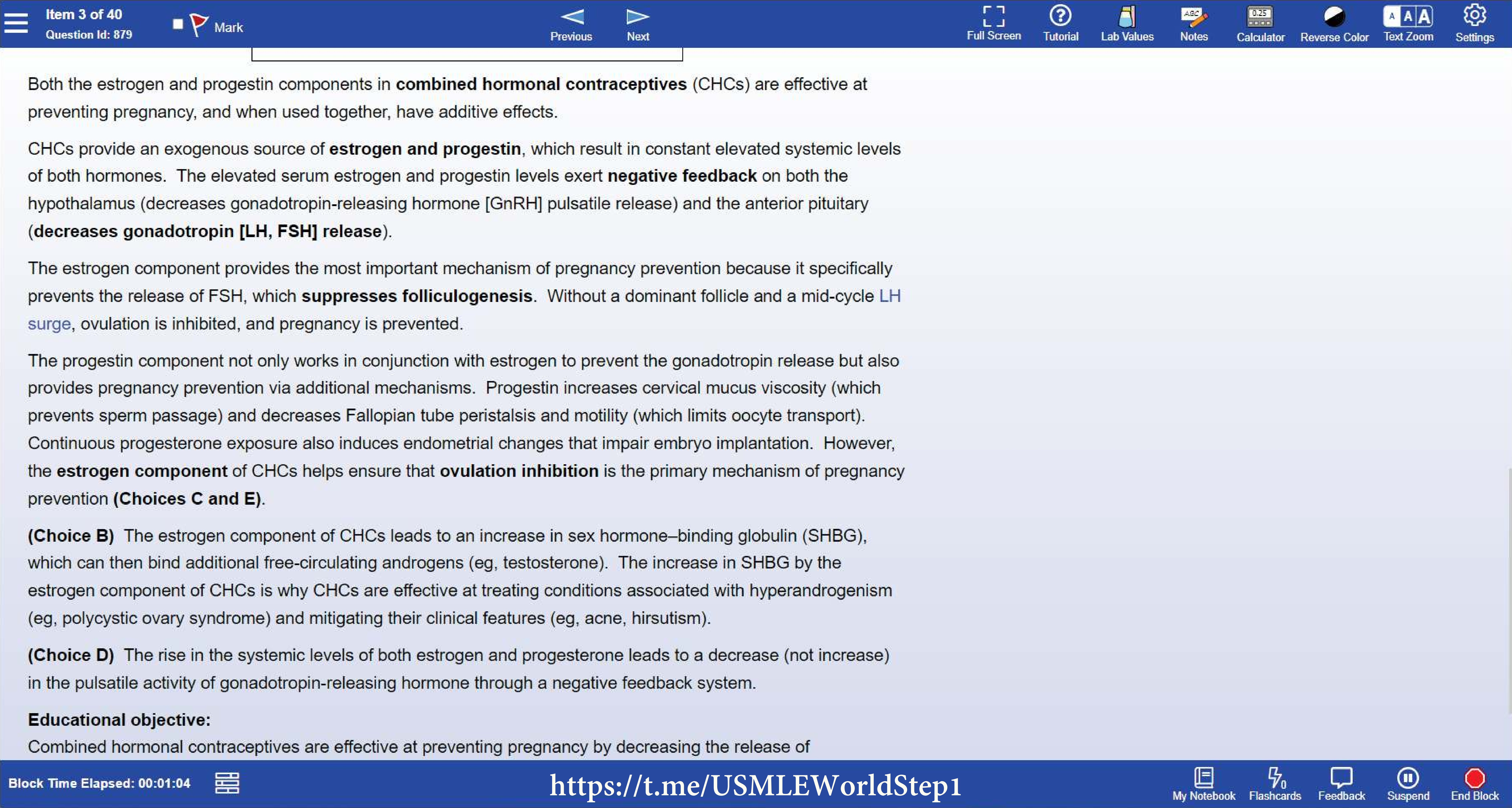
Contraceptives

Methods	Primary mechanism of action
Systemic progestins • Combined hormonal contraceptive (eg, pill, transdermal patch, vaginal ring) • Progestin implant/injection	Suppresses GnRH & pituitary gonadotropin secretion, inhibiting ovulation
Locally-acting progestins • Progestin-only (norethindrone) pill • Levonorgestrel IUD	Thickens cervical mucus, impairing sperm penetration
• Copper IUD	Creates chronic cytotoxic inflammatory response in uterus, impairing sperm migration

Combined = the combination of ethinyl estradiol & a progestin;
GnRH = gonadotropin-releasing hormone; **IUD** = intrauterine device.

Both the estrogen and progestin components in **combined hormonal contraceptives** (CHCs) are effective at



Both the estrogen and progestin components in **combined hormonal contraceptives** (CHCs) are effective at preventing pregnancy, and when used together, have additive effects.

CHCs provide an exogenous source of **estrogen and progestin**, which result in constant elevated systemic levels of both hormones. The elevated serum estrogen and progestin levels exert **negative feedback** on both the hypothalamus (decreases gonadotropin-releasing hormone [GnRH] pulsatile release) and the anterior pituitary (**decreases gonadotropin [LH, FSH] release**).

The estrogen component provides the most important mechanism of pregnancy prevention because it specifically prevents the release of FSH, which **suppresses folliculogenesis**. Without a dominant follicle and a mid-cycle LH surge, ovulation is inhibited, and pregnancy is prevented.

The progestin component not only works in conjunction with estrogen to prevent the gonadotropin release but also provides pregnancy prevention via additional mechanisms. Progestin increases cervical mucus viscosity (which prevents sperm passage) and decreases Fallopian tube peristalsis and motility (which limits oocyte transport). Continuous progesterone exposure also induces endometrial changes that impair embryo implantation. However, the **estrogen component** of CHCs helps ensure that **ovulation inhibition** is the primary mechanism of pregnancy prevention **(Choices C and E)**.

(Choice B) The estrogen component of CHCs leads to an increase in sex hormone–binding globulin (SHBG), which can then bind additional free-circulating androgens (eg, testosterone). The increase in SHBG by the estrogen component of CHCs is why CHCs are effective at treating conditions associated with hyperandrogenism (eg, polycystic ovary syndrome) and mitigating their clinical features (eg, acne, hirsutism).

(Choice D) The rise in the systemic levels of both estrogen and progesterone leads to a decrease (not increase) in the pulsatile activity of gonadotropin-releasing hormone through a negative feedback system.

Educational objective:

Combined hormonal contraceptives are effective at preventing pregnancy by decreasing the release of

CHCs provide an exogenous source of **estrogen and progestin**, which result in constant elevated systemic levels of both hormones. The elevated serum estrogen and progestin levels exert **negative feedback** on both the hypothalamus (decreases gonadotropin-releasing hormone [GnRH] pulsatile release) and the anterior pituitary (**decreases gonadotropin [LH, FSH] release**).

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Educational objective:
Combined hormonal contraceptives are effective at preventing pregnancy by decreasing the release of gonadotropins, which suppresses folliculogenesis and inhibits ovulation.

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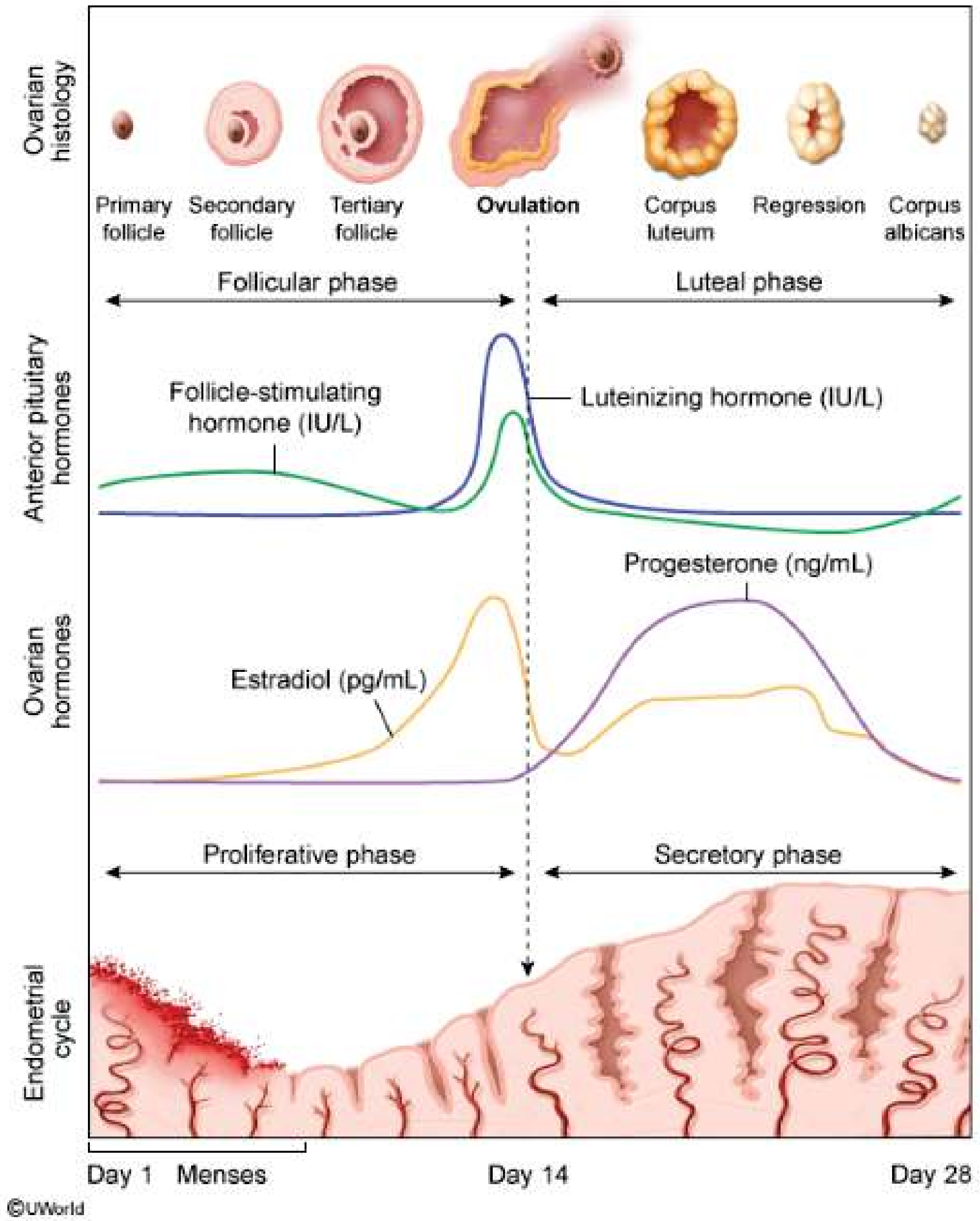
Menstrual cycle


Ovarian histology
Primary follicle
Secondary follicle
Tertiary follicle
Ovulation
Corpus luteum
Regression
Corpus albicans
Follicular phase
Luteal phase
Anterior pituitary hormones
Follicle-stimulating hormone (IU/L)
Luteinizing hormone (IU/L)
Ovarian hormones
Progesterone (ng/mL)
Estradiol (pg/mL)
Proliferative phase
Secretory phase
Endometrial cycle
Day 1
Menses
Day 14
Day 28
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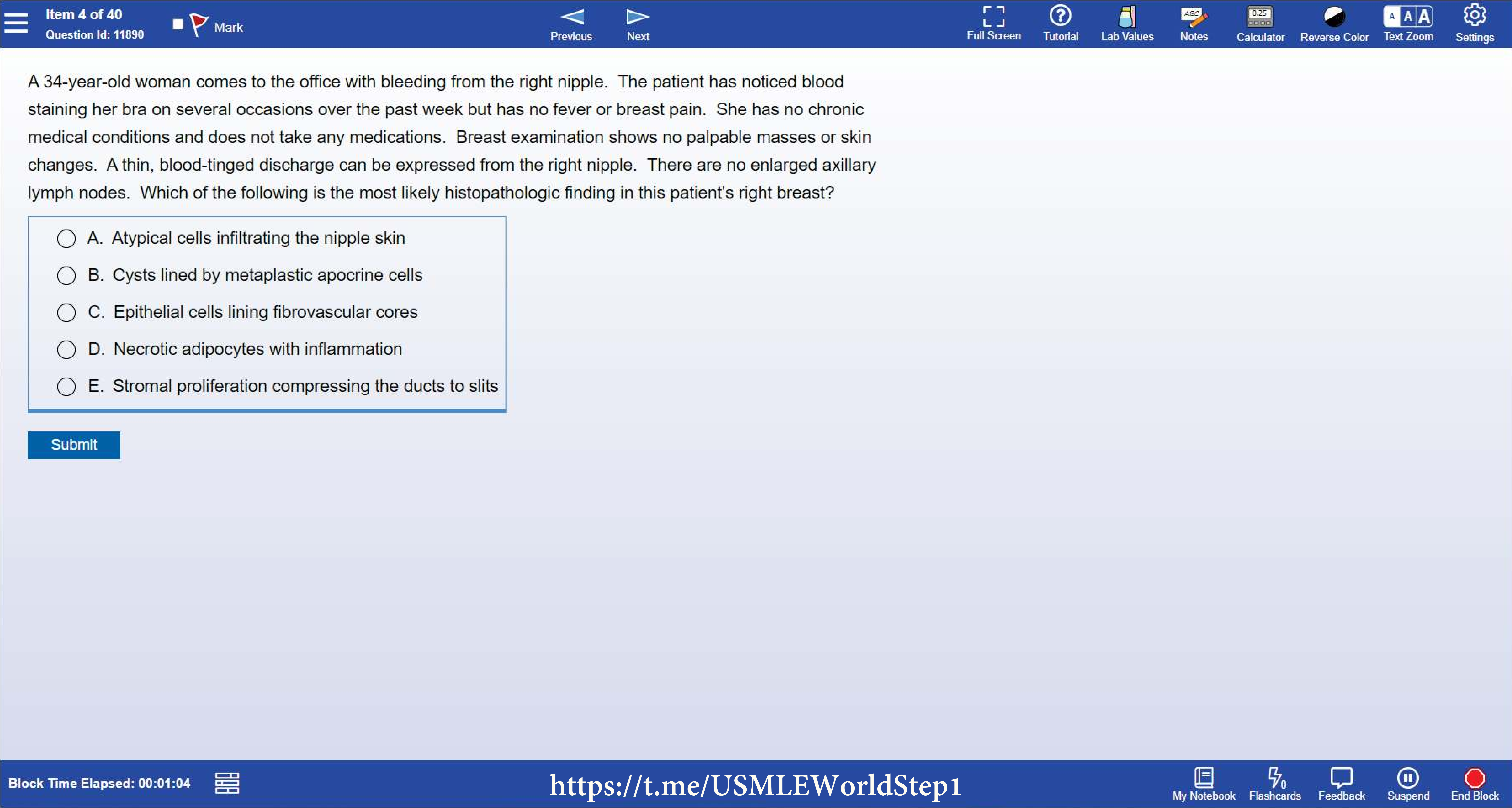
(Choice D) The rise in the systemic levels of both estrogen and progesterone leads to a decrease (not increase)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A 34-year-old woman comes to the office with bleeding from the right nipple. The patient has noticed blood staining her bra on several occasions over the past week but has no fever or breast pain. She has no chronic medical conditions and does not take any medications. Breast examination shows no palpable masses or skin changes. A thin, blood-tinged discharge can be expressed from the right nipple. There are no enlarged axillary lymph nodes. Which of the following is the most likely histopathologic finding in this patient's right breast?

○ A. Atypical cells infiltrating the nipple skin
○ B. Cysts lined by metaplastic apocrine cells
○ C. Epithelial cells lining fibrovascular cores
○ D. Necrotic adipocytes with inflammation
○ E. Stromal proliferation compressing the ducts to slits

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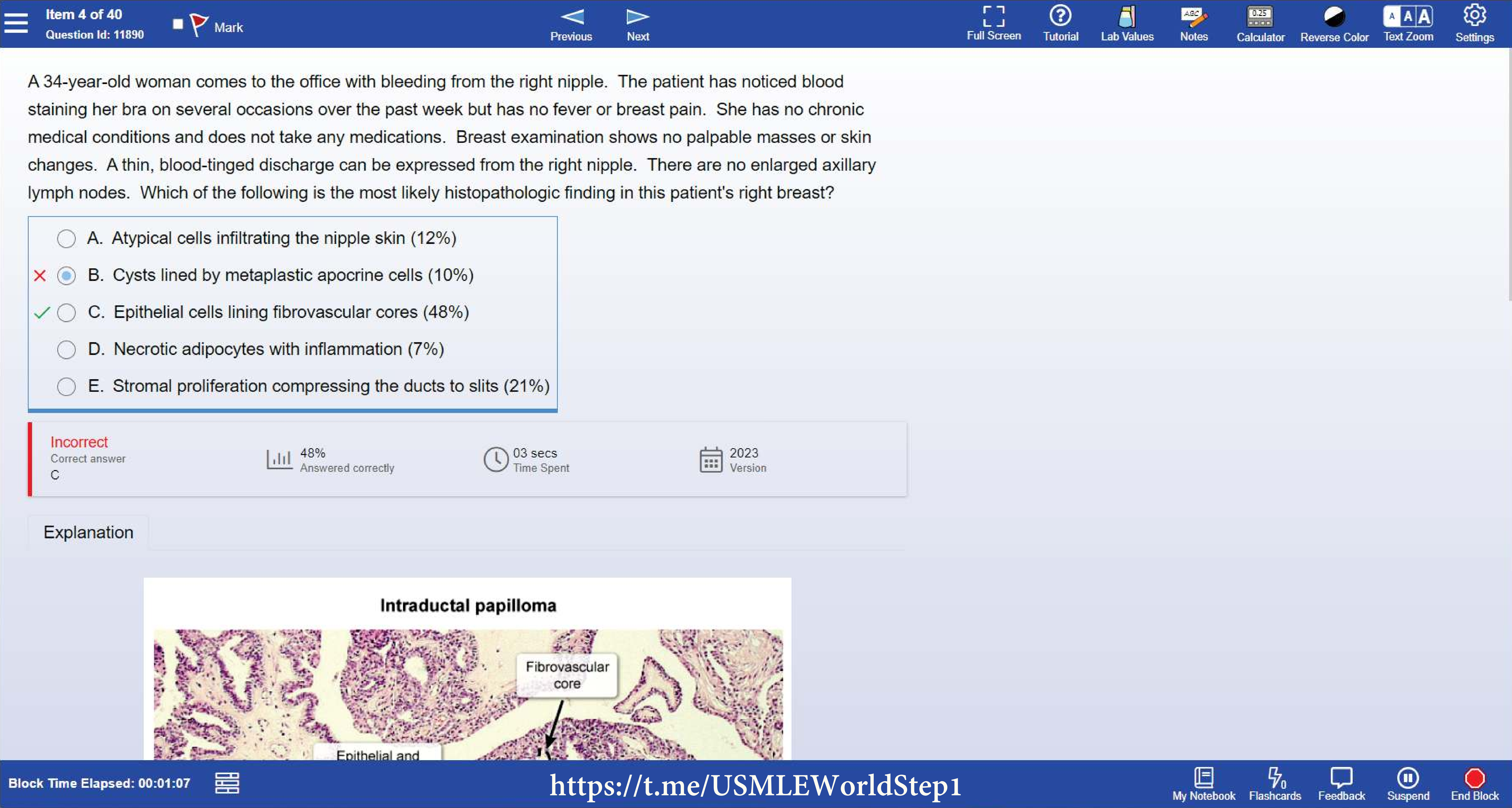
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○ A. Atypical cells infiltrating the nipple skin (12%)

✗ ● B. Cysts lined by metaplastic apocrine cells (10%)

✓ ○ C. Epithelial cells lining fibrovascular cores (48%)

○ D. Necrotic adipocytes with inflammation (7%)

○ E. Stromal proliferation compressing the ducts to slits (21%)

Incorrect
Correct answer
C

48%
Answered correctly

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Explanation

Intraductal papilloma

Fibrovascular core
Epithelial and

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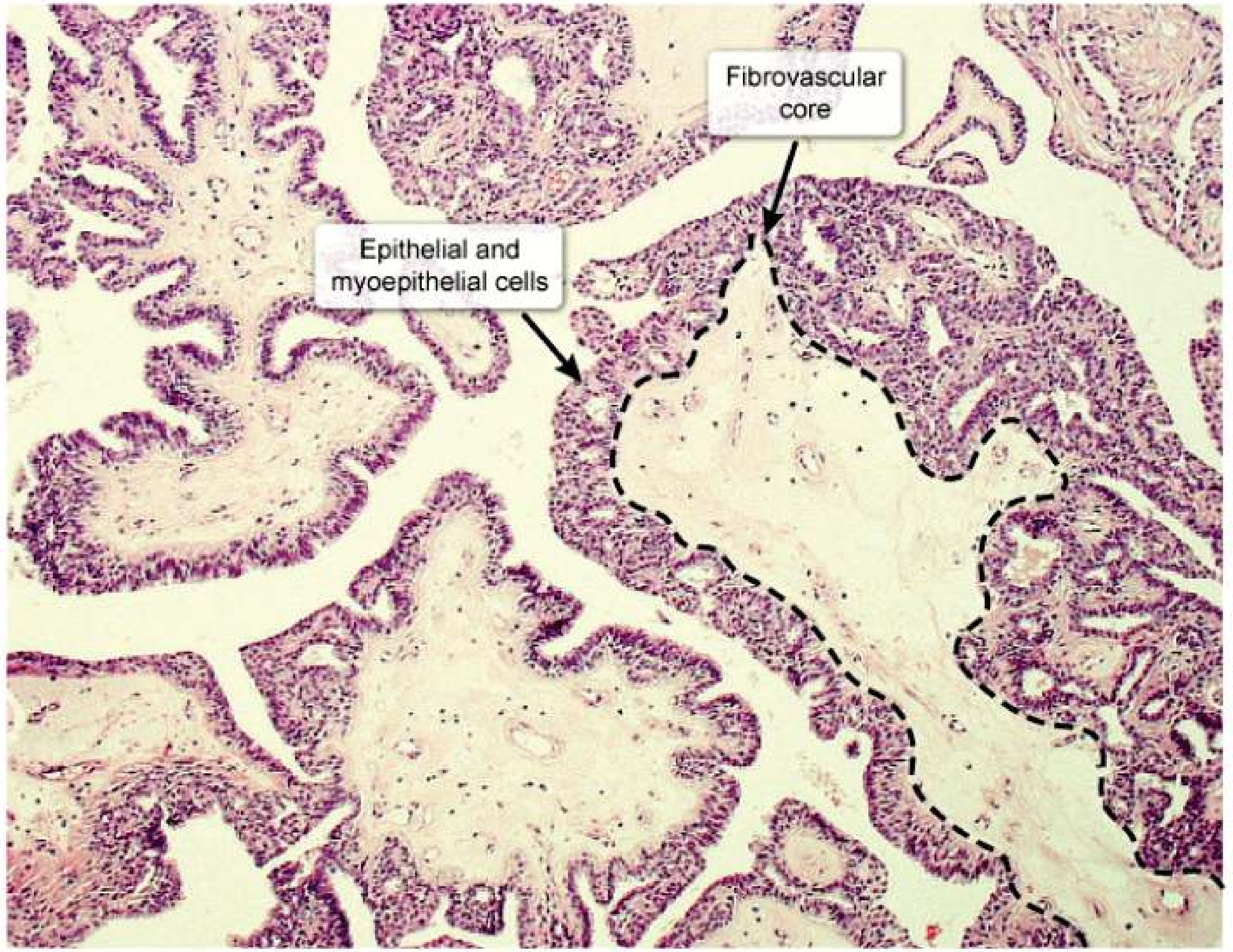
Intraductal papilloma


Fibrovascular core
Epithelial and myoepithelial cells

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Papillary architecture: fibrovascular core lined by epithelial cells

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Nipple discharge can be physiologic (ie, bilateral, nonbloody or milky, without masses or skin changes) or

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Nipple discharge can be physiologic (ie, bilateral, nonbloody or milky, without masses or skin changes) or pathologic (ie, **bloody** or serosanguineous and **unilateral** with or without palpable masses and skin changes).

The most common cause of pathologic nipple discharge is an **intraductal papilloma**, which classically presents as a unilateral, bloody nipple discharge with no associated breast masses, skin changes, or axillary lymphadenopathy. Although most cases of intraductal papilloma are benign, all patients with pathologic nipple discharge require evaluation with imaging (eg, mammogram or ultrasound, depending upon age) and possibly with biopsy. On microscopy, intraductal papilloma shows **epithelial and myoepithelial cells lining fibrovascular cores** forming papillae within a duct or cyst wall. The bloody discharge results from twisting of the vascular stalk of the papilloma in the duct.

(Choice A) Paget disease of the breast occurs due to the ductal spread of atypical malignant cells to the nipple epidermis. Although patients may have bloody nipple discharge, they also have a unilateral erythematous, intensely pruritic, ulcerative lesion over the nipple and areola, which is not seen in this patient.

(Choice B) Fibrocystic changes of the breast may show cysts with or without metaplasia and areas of fibrosis. Patients with fibrocystic changes typically have cyclic breast pain, not nipple discharge.

(Choice D) Fat necrosis typically presents as an irregular breast mass with no associated nipple discharge after localized trauma or biopsy. Microscopy may show adipocytes undergoing necrosis with inflammation, including macrophages and giant cells.

(Choice E) Fibroadenomas are small, firm, and mobile breast masses that occur due to proliferation of breast stroma and ducts. Fibroadenomas do not typically cause bloody nipple discharge. Microscopic examination shows stromal proliferation compressing the ducts to slits.

Educational objective:

Intraductal papilloma is characterized by epithelial and myoepithelial cells lining fibrovascular cores in a cyst wall or duct. It is the most common cause of bloody nipple discharge and typically presents without breast masses or skin changes.

Nipple discharge can be physiologic (ie, bilateral, nonbloody or milky, without masses or skin changes) or

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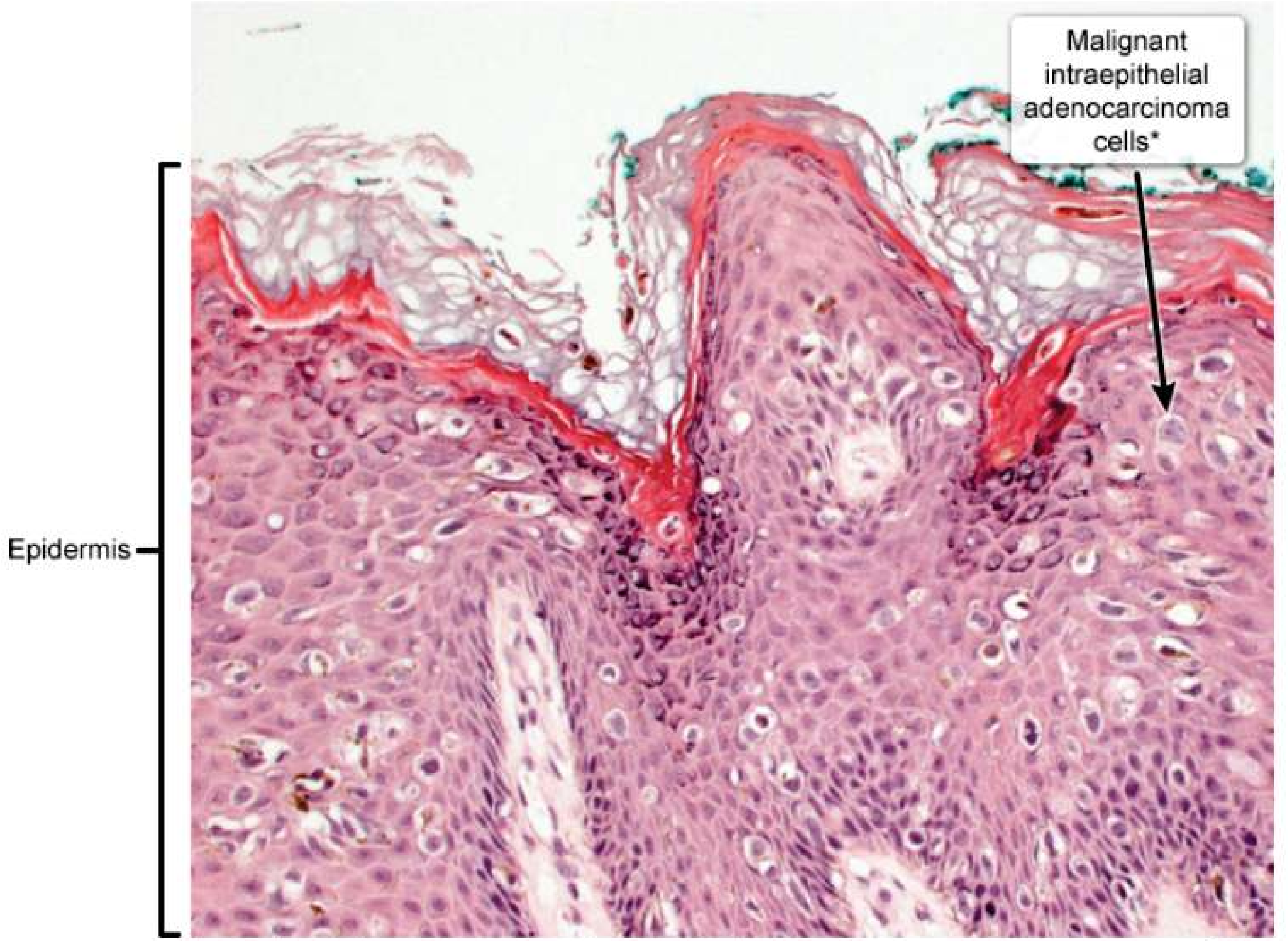
Paget disease of the breast



*Large cells with abundant cytoplasm and prominent nucleoli.

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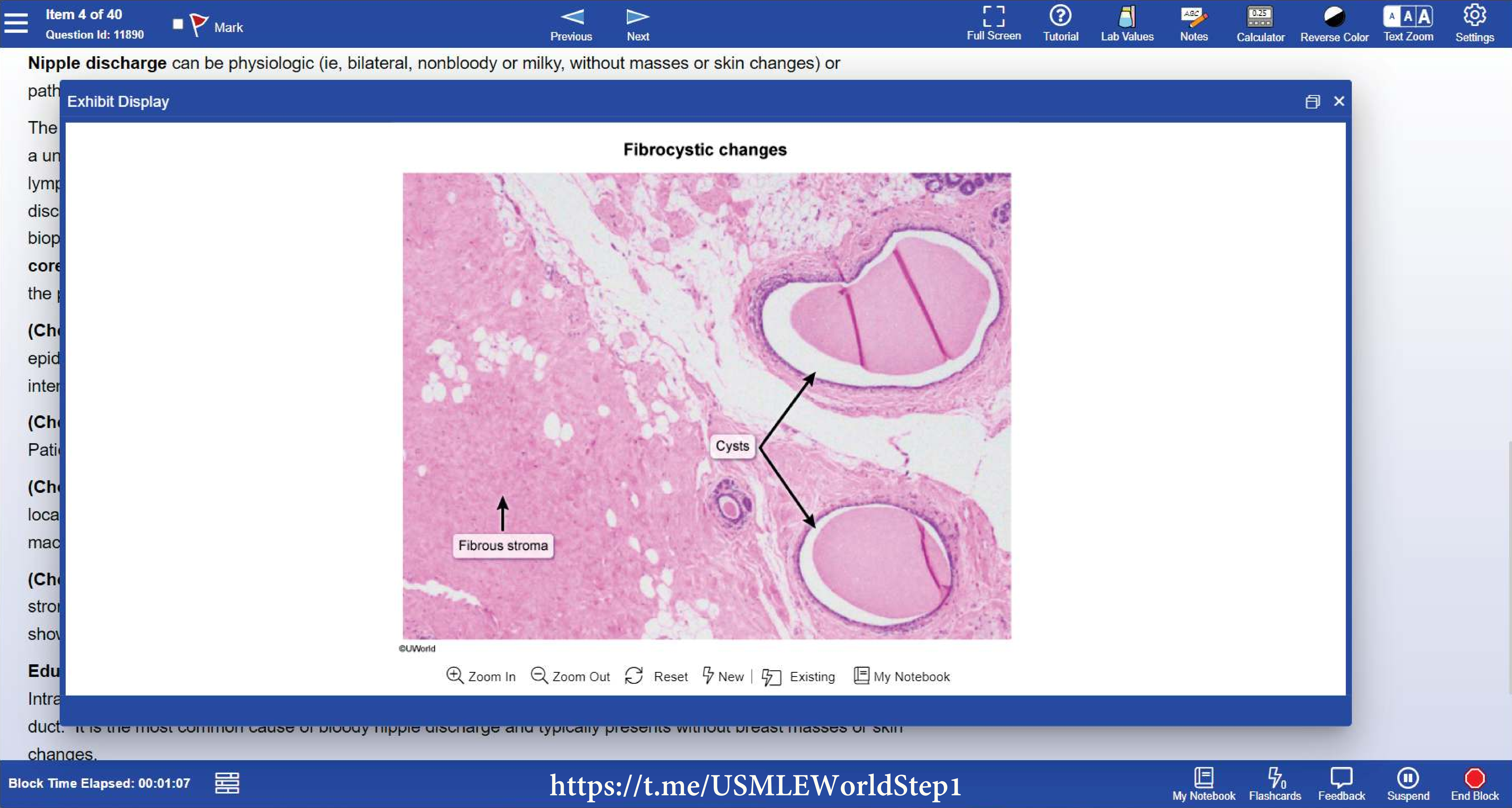
duct. It is the most common cause of bloody nipple discharge and typically presents without breast masses or skin changes.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Fibrocystic changes

Cysts
Fibrous stroma

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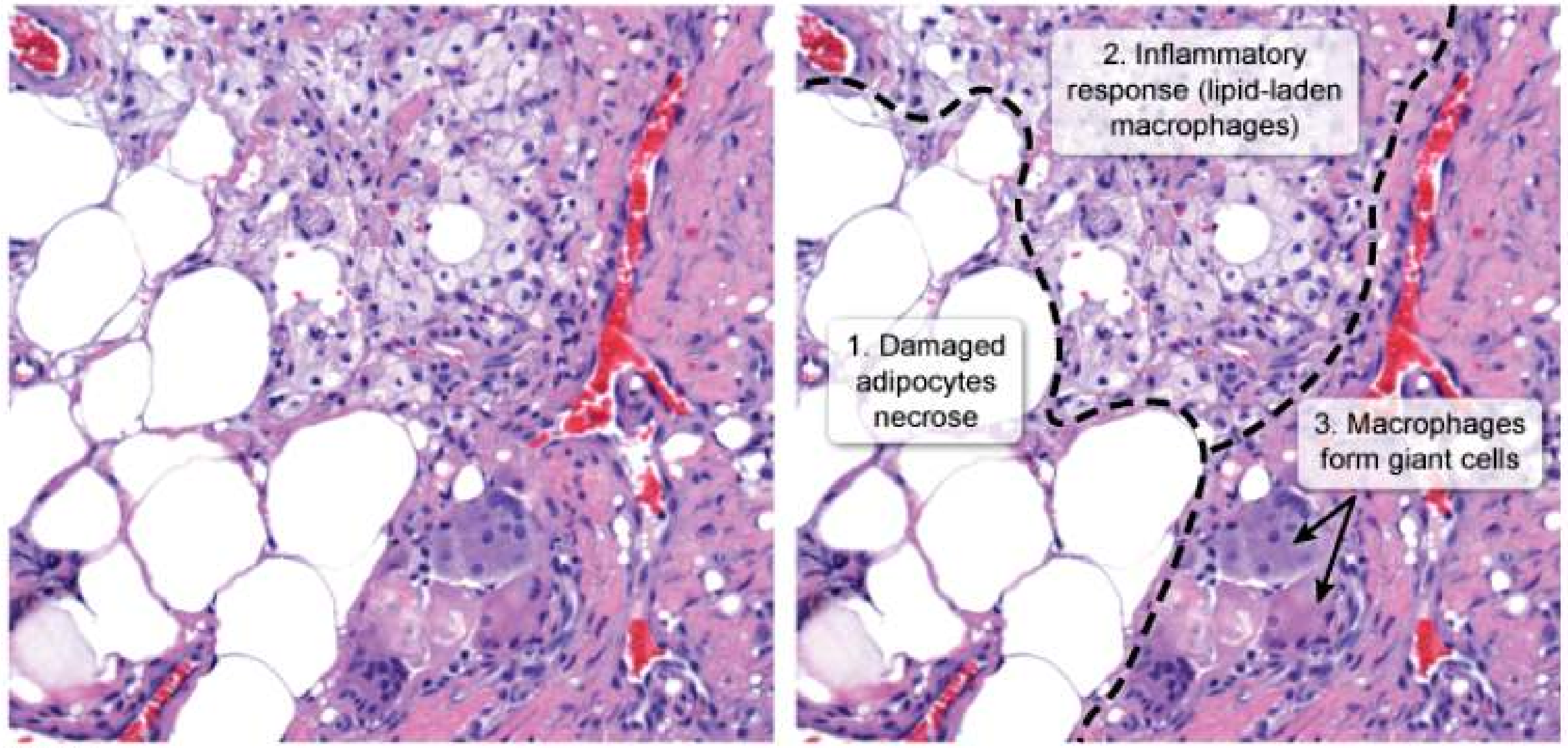
Fat necrosis


2. Inflammatory response (lipid-laden macrophages)
1. Damaged adipocytes necrose
3. Macrophages form giant cells

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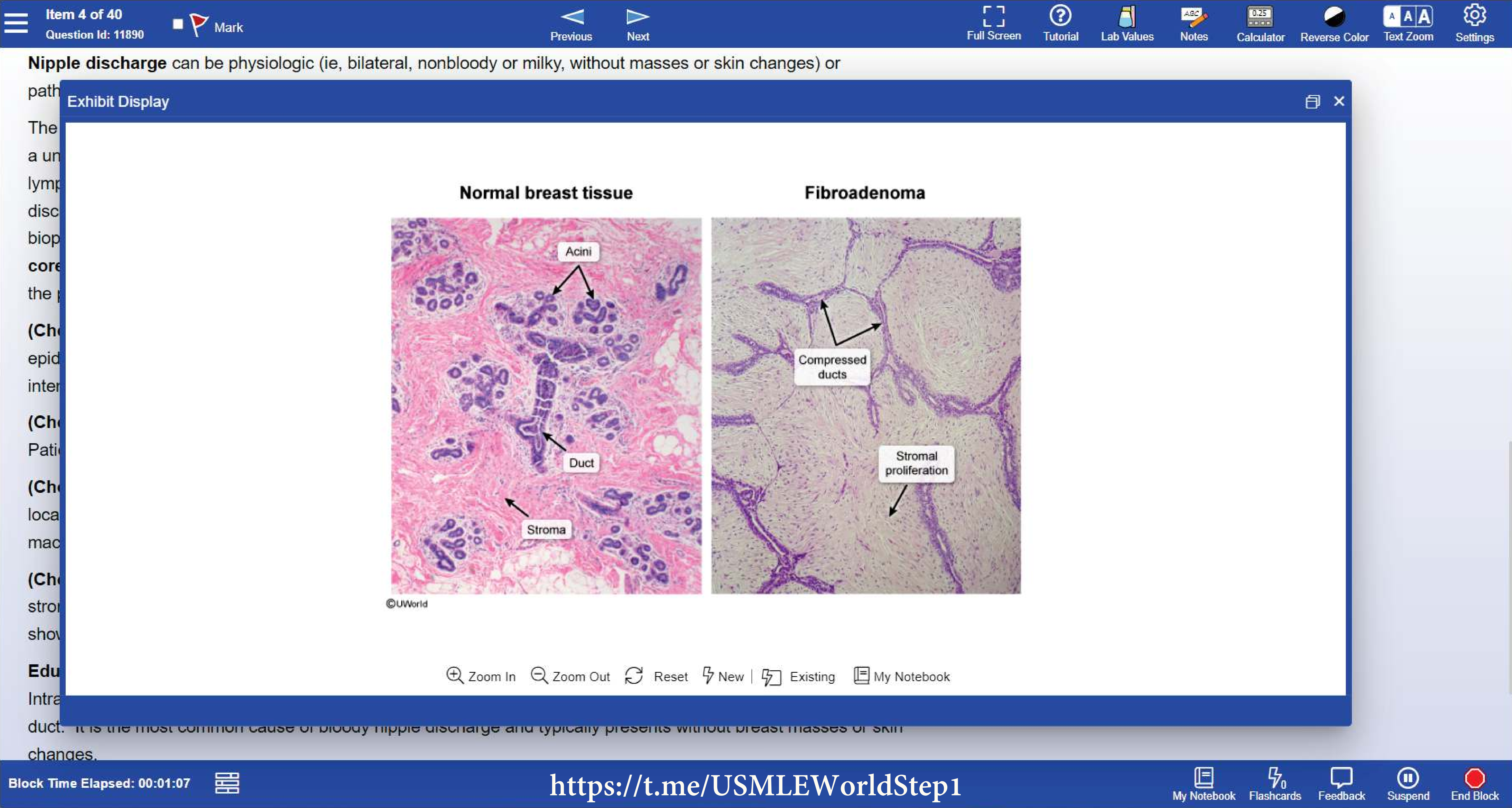

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Nipple discharge can be physiologic (ie, bilateral, nonbloody or milky, without masses or skin changes) or path

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duct. It is the most common cause of bloody nipple discharge and typically presents without breast masses or skin changes.

Exhibit Display

Normal breast tissue **Fibroadenoma**

Acini
Duct
Stroma
Compressed ducts
Stromal proliferation

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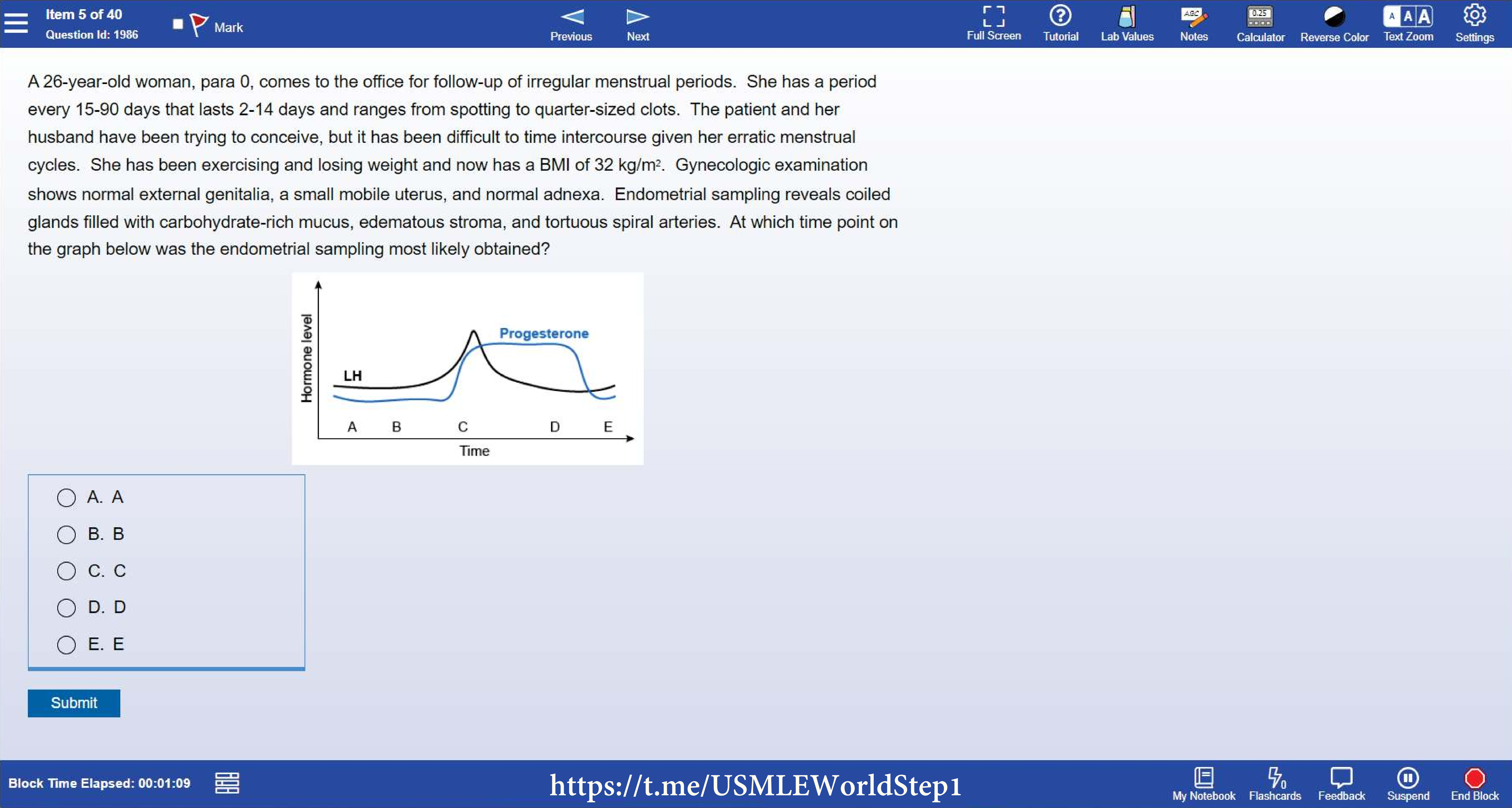
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A 26-year-old woman, para 0, comes to the office for follow-up of irregular menstrual periods. She has a period every 15-90 days that lasts 2-14 days and ranges from spotting to quarter-sized clots. The patient and her husband have been trying to conceive, but it has been difficult to time intercourse given her erratic menstrual cycles. She has been exercising and losing weight and now has a BMI of 32 kg/m^2. Gynecologic examination shows normal external genitalia, a small mobile uterus, and normal adnexa. Endometrial sampling reveals coiled glands filled with carbohydrate-rich mucus, edematous stroma, and tortuous spiral arteries. At which time point on the graph below was the endometrial sampling most likely obtained?

Hormone level
Progesterone
LH
A
B
C
D
E
Time

○ A. A

○ B. B

○ C. C

○ D. D

○ E. E

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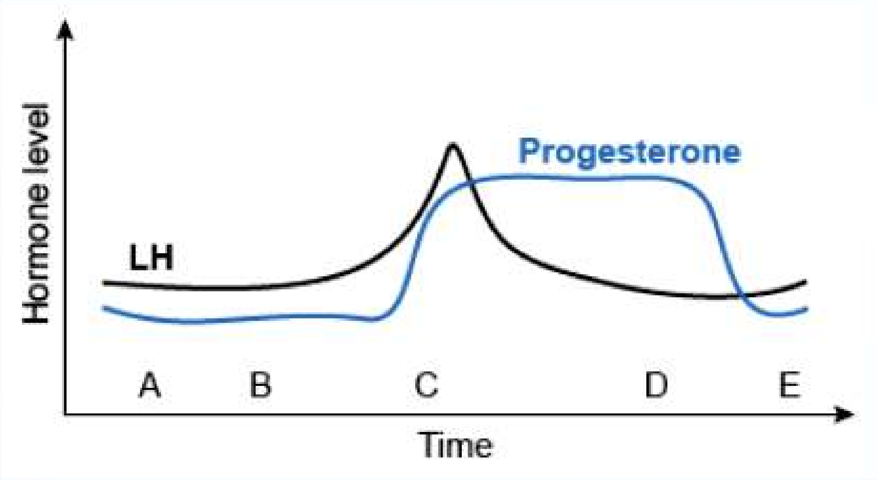

○ A. A (0%)

✗ ● B. B (2%)

○ C. C (12%)

✓ ○ D. D (82%)

○ E. E (1%)

Incorrect
Correct answer
D

82%
Answered correctly

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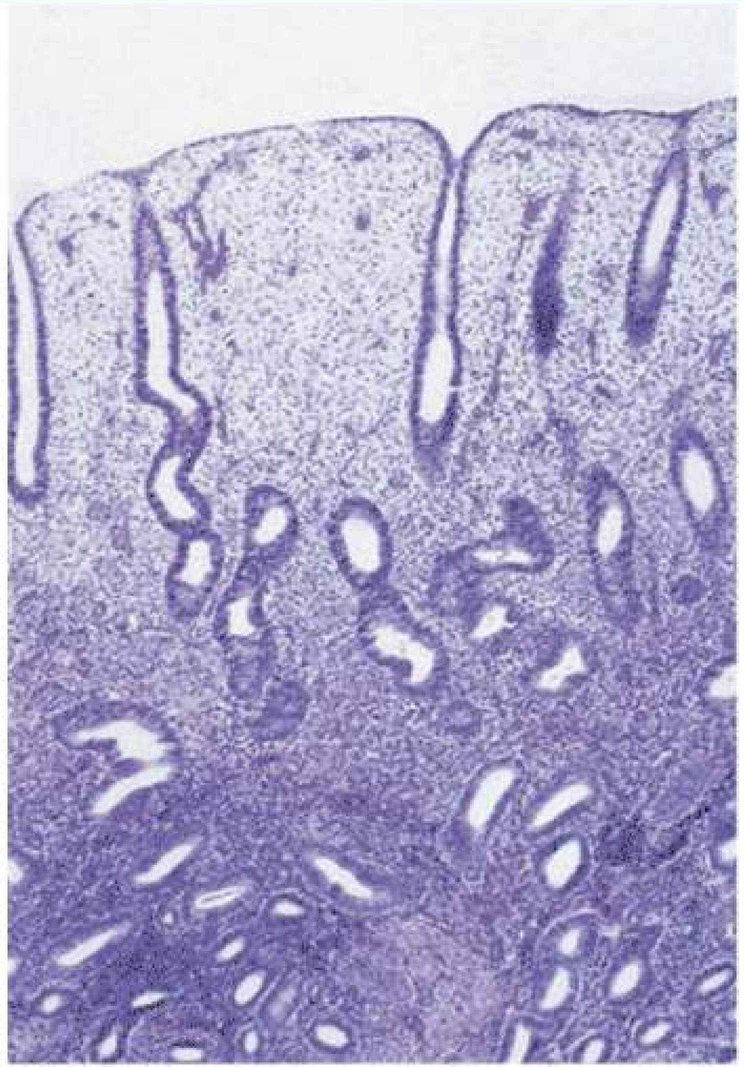
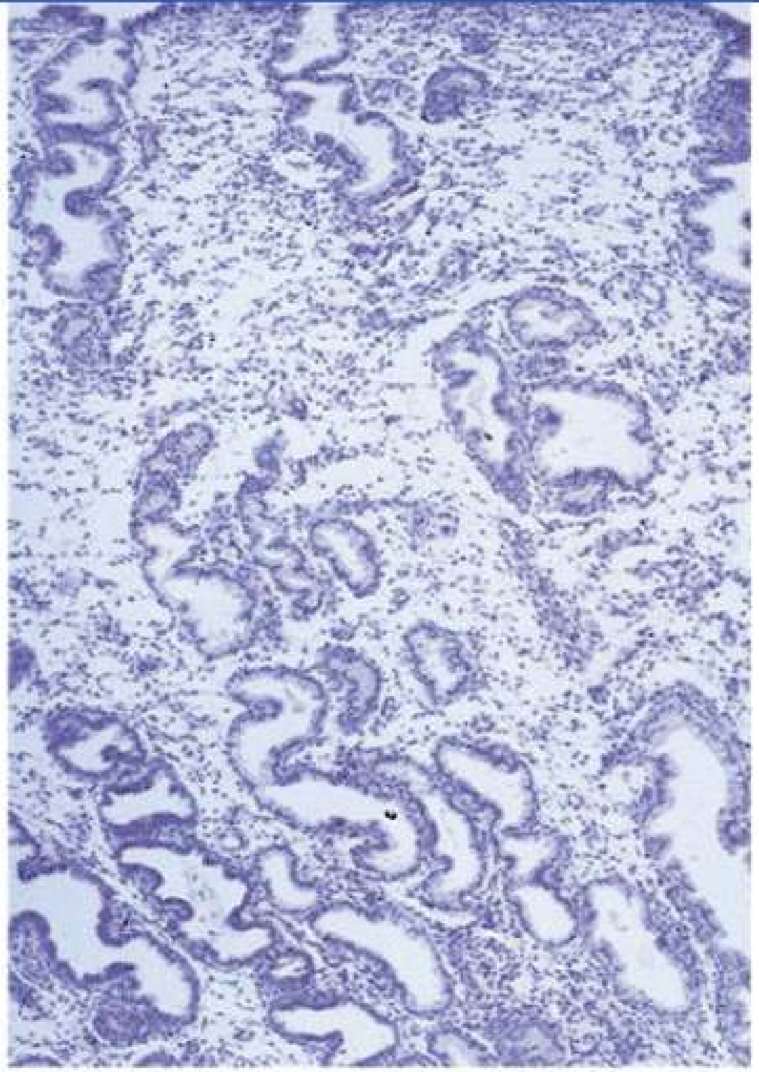


Mid-proliferative phase endometrium (day 7). The endometrium demonstrates uniform development, with a gland:stroma ratio of less than 1:1. The glands are straight and narrow, and contain small lumens.



Mid-secretory phase endometrium (day 21). The gland:stroma ratio has increased to approximately 1:1 because the amplified stromal volume is associated with marked stromal edema. The glands are dilated and coiled, and contain wide lumens.

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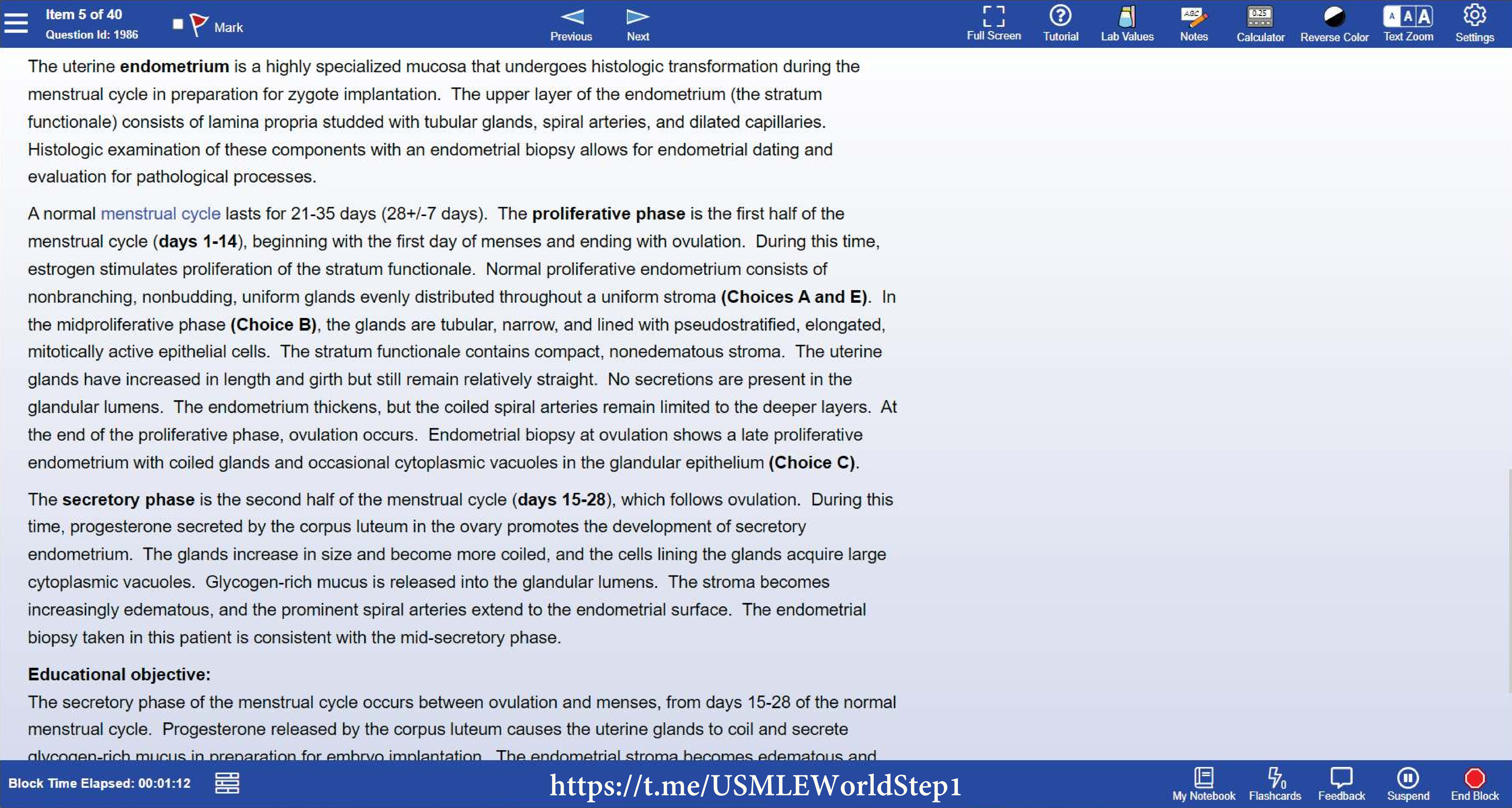
The uterine **endometrium** is a highly specialized mucosa that undergoes histologic transformation during the



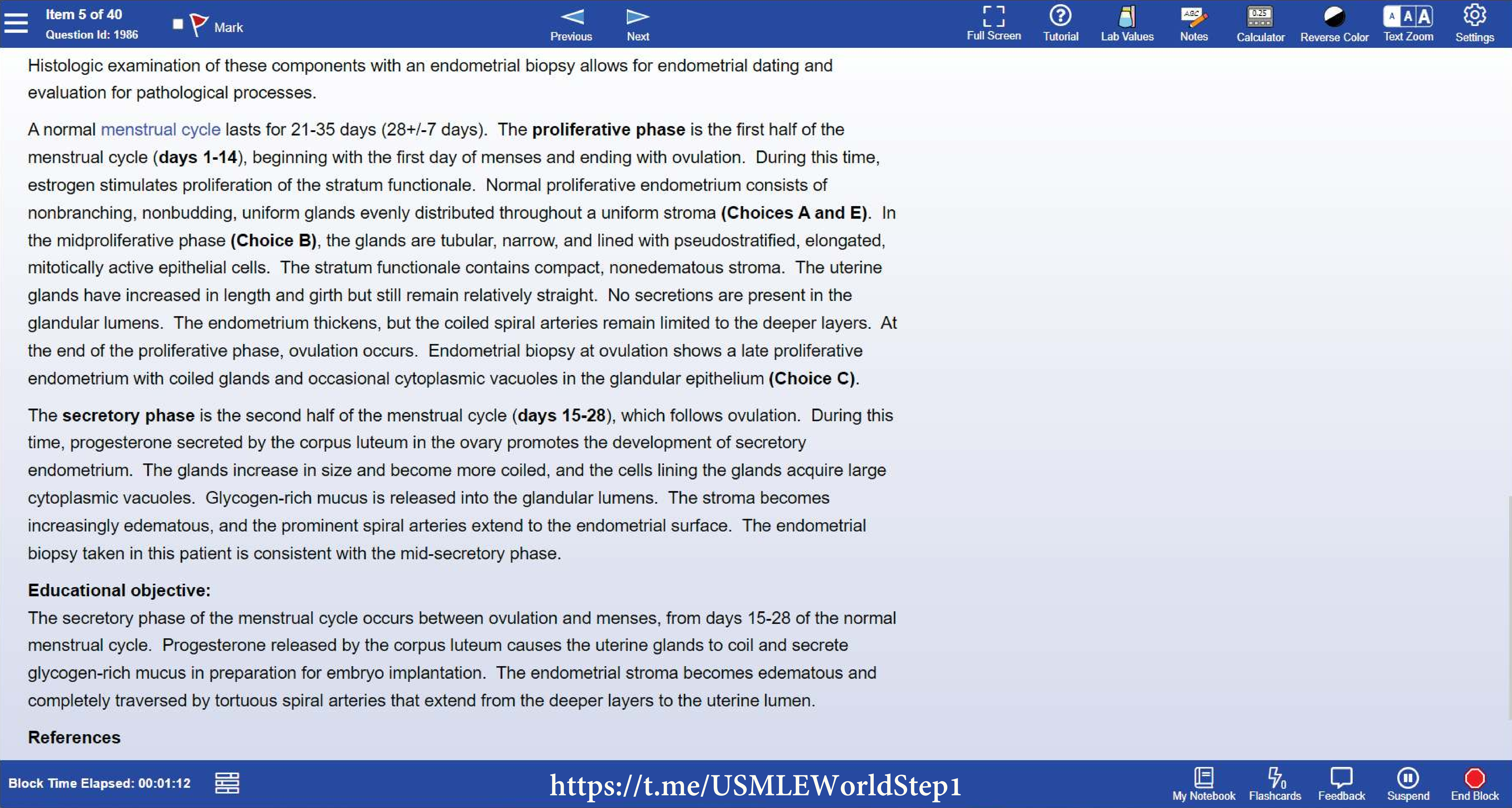
The uterine **endometrium** is a highly specialized mucosa that undergoes histologic transformation during the menstrual cycle in preparation for zygote implantation. The upper layer of the endometrium (the stratum functionale) consists of lamina propria studded with tubular glands, spiral arteries, and dilated capillaries. Histologic examination of these components with an endometrial biopsy allows for endometrial dating and evaluation for pathological processes.

A normal menstrual cycle lasts for 21-35 days (28+/-7 days). The **proliferative phase** is the first half of the menstrual cycle (**days 1-14**), beginning with the first day of menses and ending with ovulation. During this time, estrogen stimulates proliferation of the stratum functionale. Normal proliferative endometrium consists of nonbranching, nonbudding, uniform glands evenly distributed throughout a uniform stroma **(Choices A and E)**. In the midproliferative phase **(Choice B)**, the glands are tubular, narrow, and lined with pseudostratified, elongated, mitotically active epithelial cells. The stratum functionale contains compact, nonedematous stroma. The uterine glands have increased in length and girth but still remain relatively straight. No secretions are present in the glandular lumens. The endometrium thickens, but the coiled spiral arteries remain limited to the deeper layers. At the end of the proliferative phase, ovulation occurs. Endometrial biopsy at ovulation shows a late proliferative endometrium with coiled glands and occasional cytoplasmic vacuoles in the glandular epithelium **(Choice C)**.

The **secretory phase** is the second half of the menstrual cycle (**days 15-28**), which follows ovulation. During this time, progesterone secreted by the corpus luteum in the ovary promotes the development of secretory endometrium. The glands increase in size and become more coiled, and the cells lining the glands acquire large cytoplasmic vacuoles. Glycogen-rich mucus is released into the glandular lumens. The stroma becomes increasingly edematous, and the prominent spiral arteries extend to the endometrial surface. The endometrial biopsy taken in this patient is consistent with the mid-secretory phase.

Educational objective:

The secretory phase of the menstrual cycle occurs between ovulation and menses, from days 15-28 of the normal menstrual cycle. Progesterone released by the corpus luteum causes the uterine glands to coil and secrete glycogen-rich mucus in preparation for embryo implantation. The endometrial stroma becomes edematous and



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The secretory phase of the menstrual cycle occurs between ovulation and menses, from days 15-28 of the normal menstrual cycle. Progesterone released by the corpus luteum causes the uterine glands to coil and secrete glycogen-rich mucus in preparation for embryo implantation. The endometrial stroma becomes edematous and completely traversed by tortuous spiral arteries that extend from the deeper layers to the uterine lumen.

References

The uterine **endometrium** is a highly specialized mucosa that undergoes histologic transformation during the

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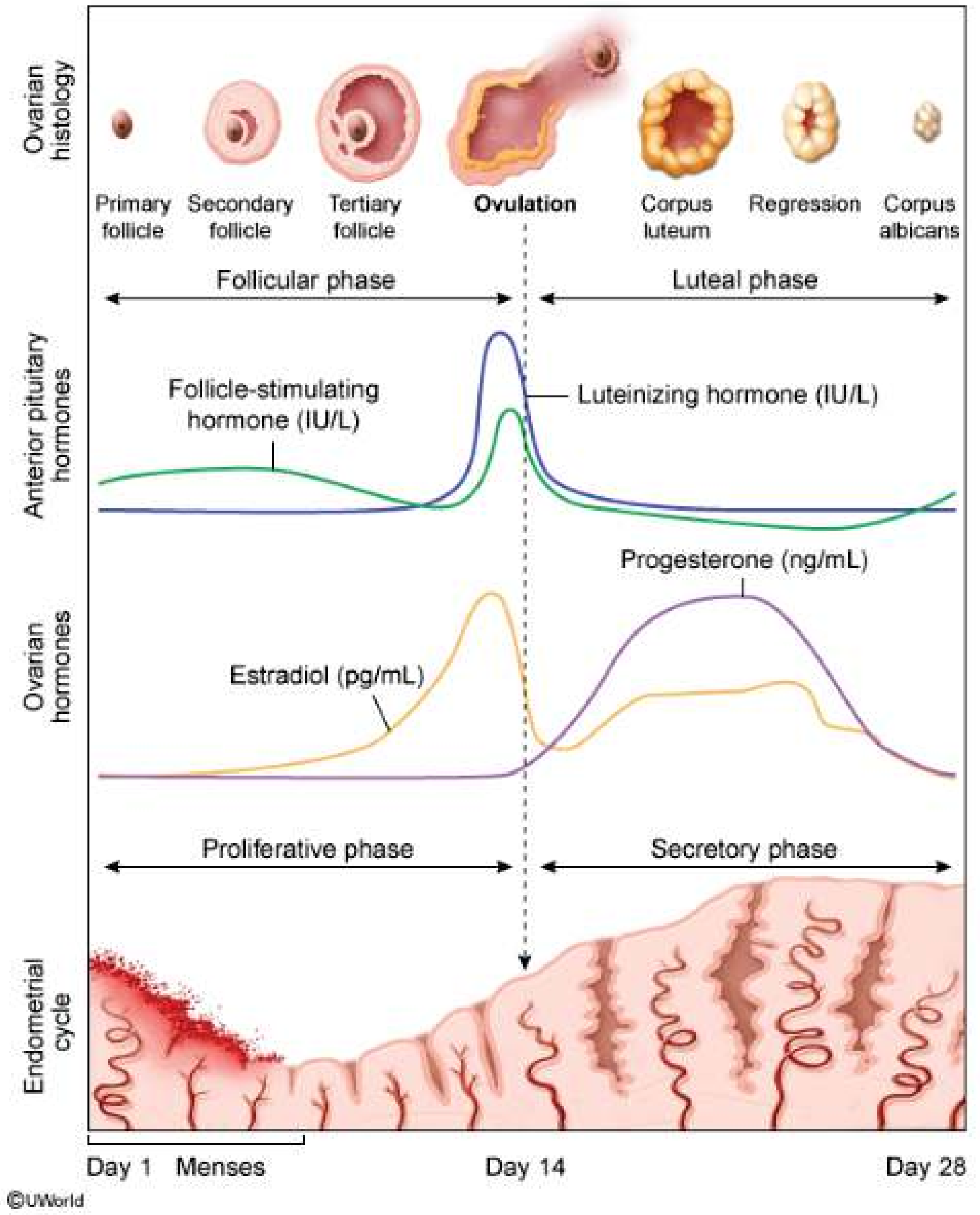
Menstrual cycle


Ovarian histology
Primary follicle
Secondary follicle
Tertiary follicle
Ovulation
Corpus luteum
Regression
Corpus albicans
Follicular phase
Luteal phase
Anterior pituitary hormones
Follicle-stimulating hormone (IU/L)
Luteinizing hormone (IU/L)
Ovarian hormones
Progesterone (ng/mL)
Estradiol (pg/mL)
Proliferative phase
Secretory phase
Endometrial cycle
Day 1
Menses
Day 14
Day 28
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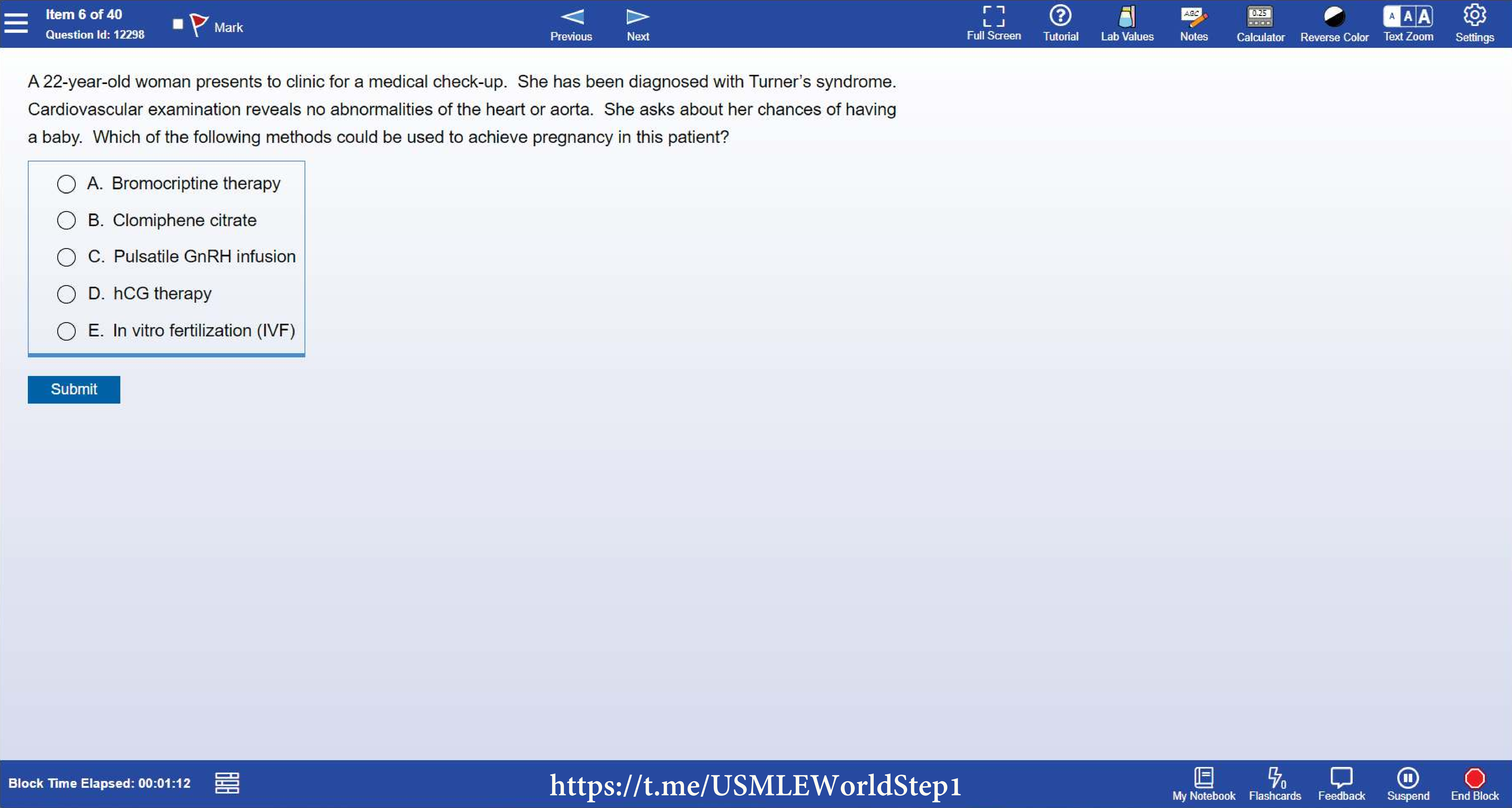
menstrual cycle. Progesterone released by the corpus luteum causes the uterine glands to coil and secrete glycogen-rich mucus in preparation for embryo implantation. The endometrial stroma becomes edematous and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A 22-year-old woman presents to clinic for a medical check-up. She has been diagnosed with Turner's syndrome. Cardiovascular examination reveals no abnormalities of the heart or aorta. She asks about her chances of having a baby. Which of the following methods could be used to achieve pregnancy in this patient?

○ A. Bromocriptine therapy
○ B. Clomiphene citrate
○ C. Pulsatile GnRH infusion
○ D. hCG therapy
○ E. In vitro fertilization (IVF)

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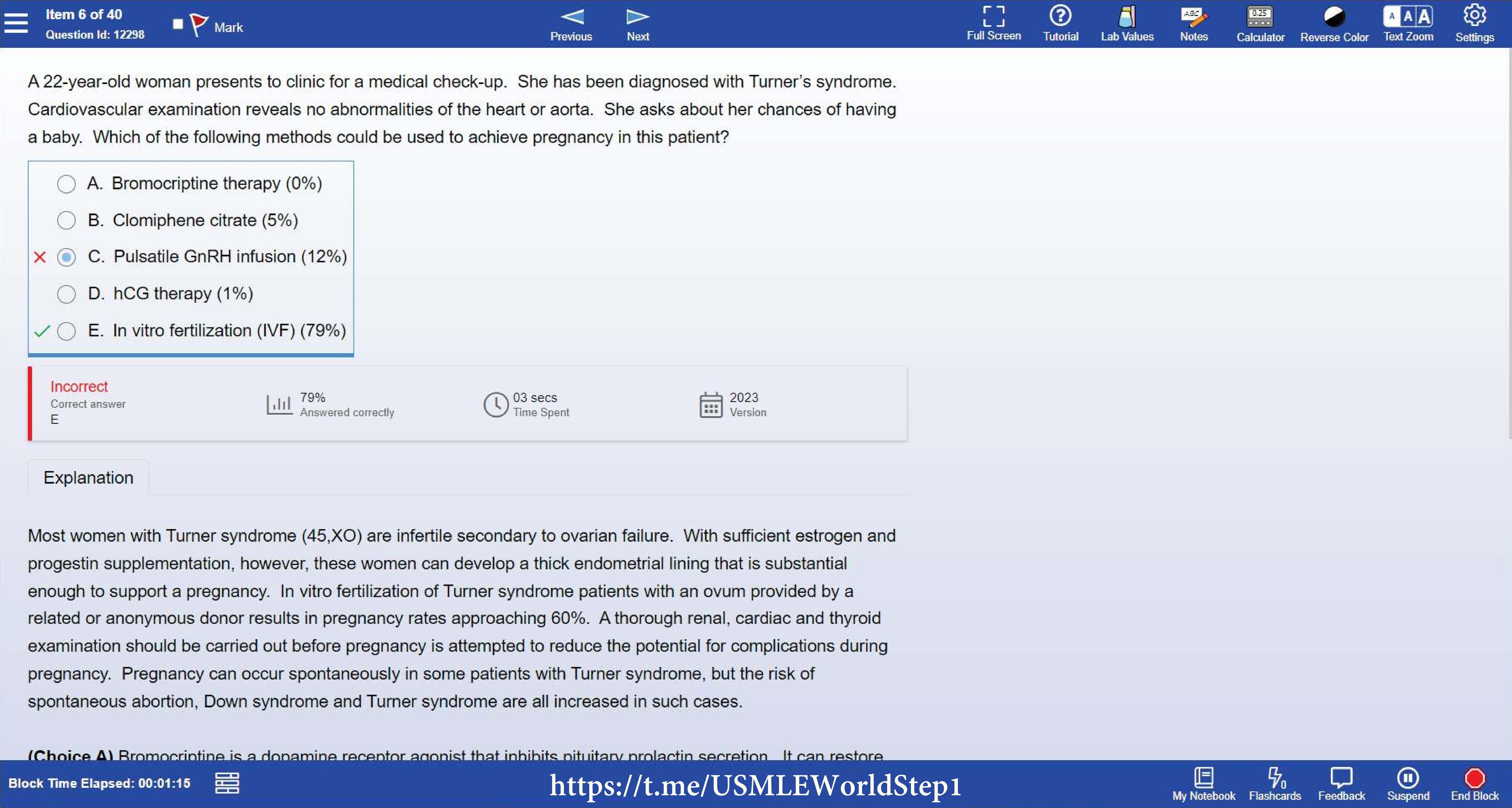
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○ A. Bromocriptine therapy (0%)
○ B. Clomiphene citrate (5%)
✗ ● C. Pulsatile GnRH infusion (12%)
○ D. hCG therapy (1%)
✓ ○ E. In vitro fertilization (IVF) (79%)

Incorrect
Correct answer
E

79%
Answered correctly

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Explanation

Most women with Turner syndrome (45,XO) are infertile secondary to ovarian failure. With sufficient estrogen and progestin supplementation, however, these women can develop a thick endometrial lining that is substantial enough to support a pregnancy. In vitro fertilization of Turner syndrome patients with an ovum provided by a related or anonymous donor results in pregnancy rates approaching 60%. A thorough renal, cardiac and thyroid examination should be carried out before pregnancy is attempted to reduce the potential for complications during pregnancy. Pregnancy can occur spontaneously in some patients with Turner syndrome, but the risk of spontaneous abortion, Down syndrome and Turner syndrome are all increased in such cases.

(Choice A) Bromocriptine is a dopamine receptor agonist that inhibits pituitary prolactin secretion. It can restore

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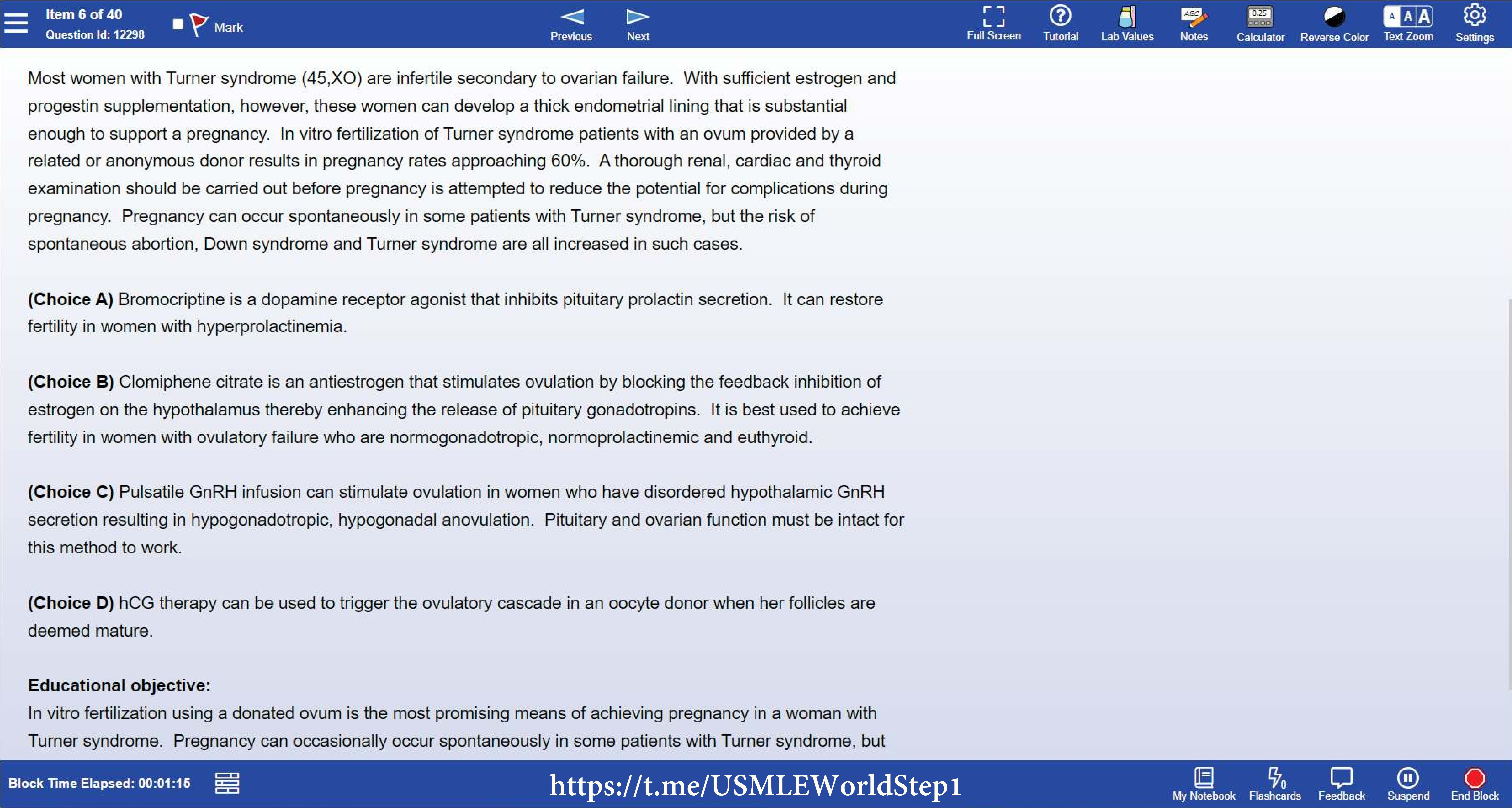
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(Choice A) Bromocriptine is a dopamine receptor agonist that inhibits pituitary prolactin secretion. It can restore fertility in women with hyperprolactinemia.

(Choice B) Clomiphene citrate is an antiestrogen that stimulates ovulation by blocking the feedback inhibition of estrogen on the hypothalamus thereby enhancing the release of pituitary gonadotropins. It is best used to achieve fertility in women with ovulatory failure who are normogonadotropic, normoprolactinemic and euthyroid.

(Choice C) Pulsatile GnRH infusion can stimulate ovulation in women who have disordered hypothalamic GnRH secretion resulting in hypogonadotropic, hypogonadal anovulation. Pituitary and ovarian function must be intact for this method to work.

(Choice D) hCG therapy can be used to trigger the ovulatory cascade in an oocyte donor when her follicles are deemed mature.

Educational objective:

In vitro fertilization using a donated ovum is the most promising means of achieving pregnancy in a woman with Turner syndrome. Pregnancy can occasionally occur spontaneously in some patients with Turner syndrome, but

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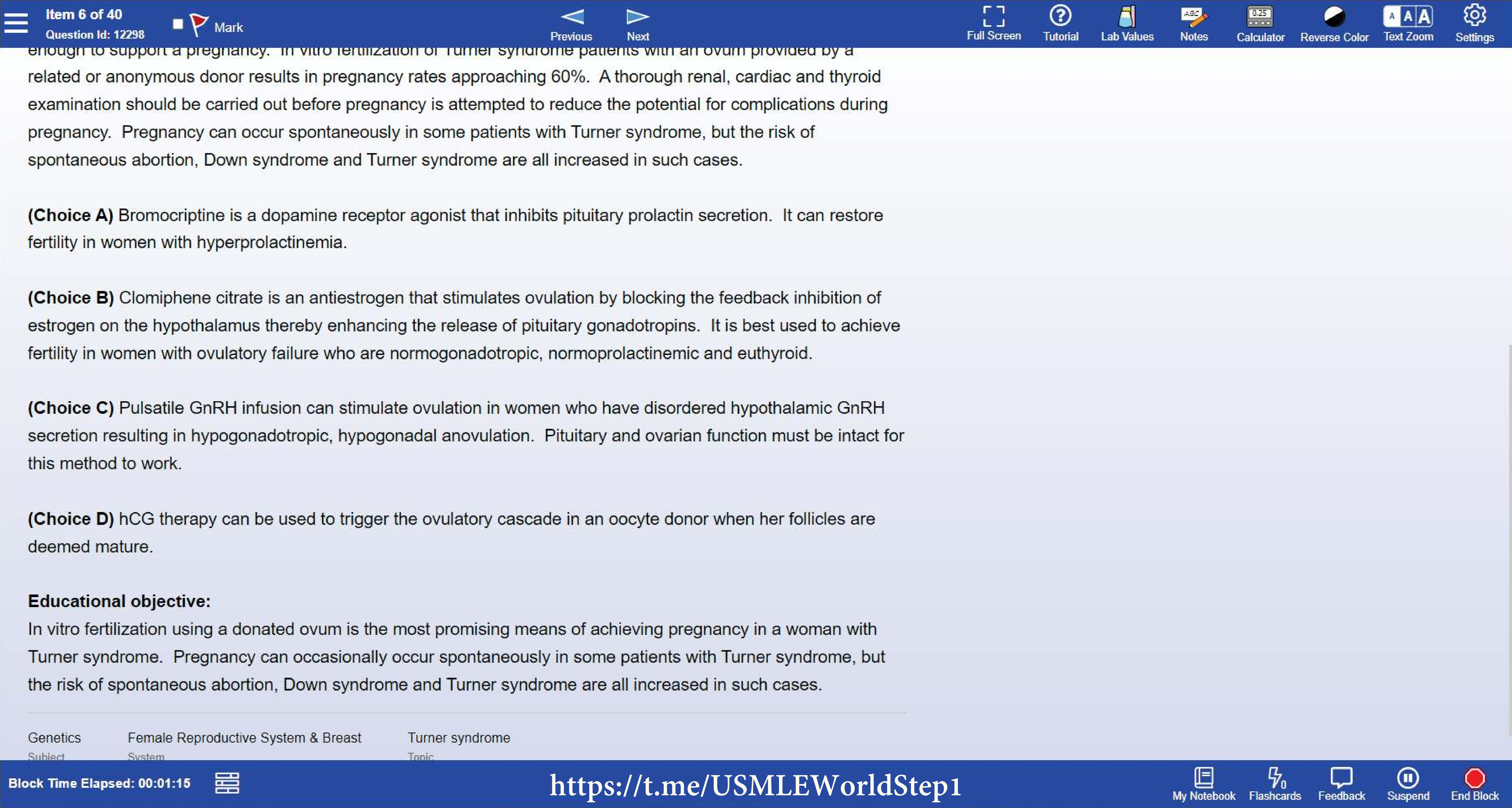
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In vitro fertilization using a donated ovum is the most promising means of achieving pregnancy in a woman with Turner syndrome. Pregnancy can occasionally occur spontaneously in some patients with Turner syndrome, but the risk of spontaneous abortion, Down syndrome and Turner syndrome are all increased in such cases.

Genetics	Female Reproductive System & Breast	Turner syndrome
Subject	System	Topic

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A 20-year-old woman comes to the office due to increasing vaginal discharge and vulvar pruritus. The patient has had vaginal discharge for the past 4 days. She is sexually active with multiple partners and uses oral contraceptive pills. Vital signs are normal. Pelvic examination is performed, and wet mount microscopy of a vaginal swab is shown in the exhibit. Which of the following is the most appropriate pharmacotherapy for this patient?

○ A. Acyclovir
○ B. Ceftriaxone
○ C. Clindamycin
○ D. Doxycycline
○ E. Fluconazole
○ F. Metronidazole

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A 20 year-old woman comes to the office due to increasing vaginal discharge and vulvar pruritus. The patient has
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pills.
shov

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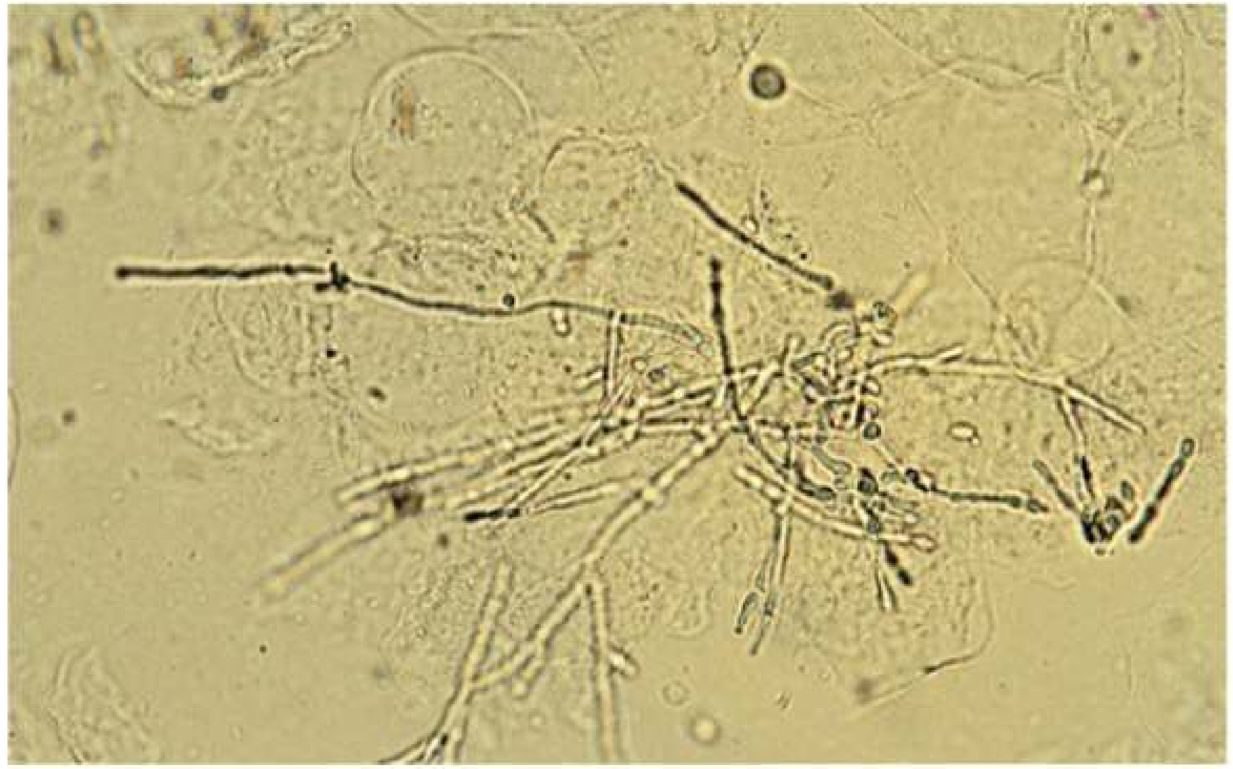

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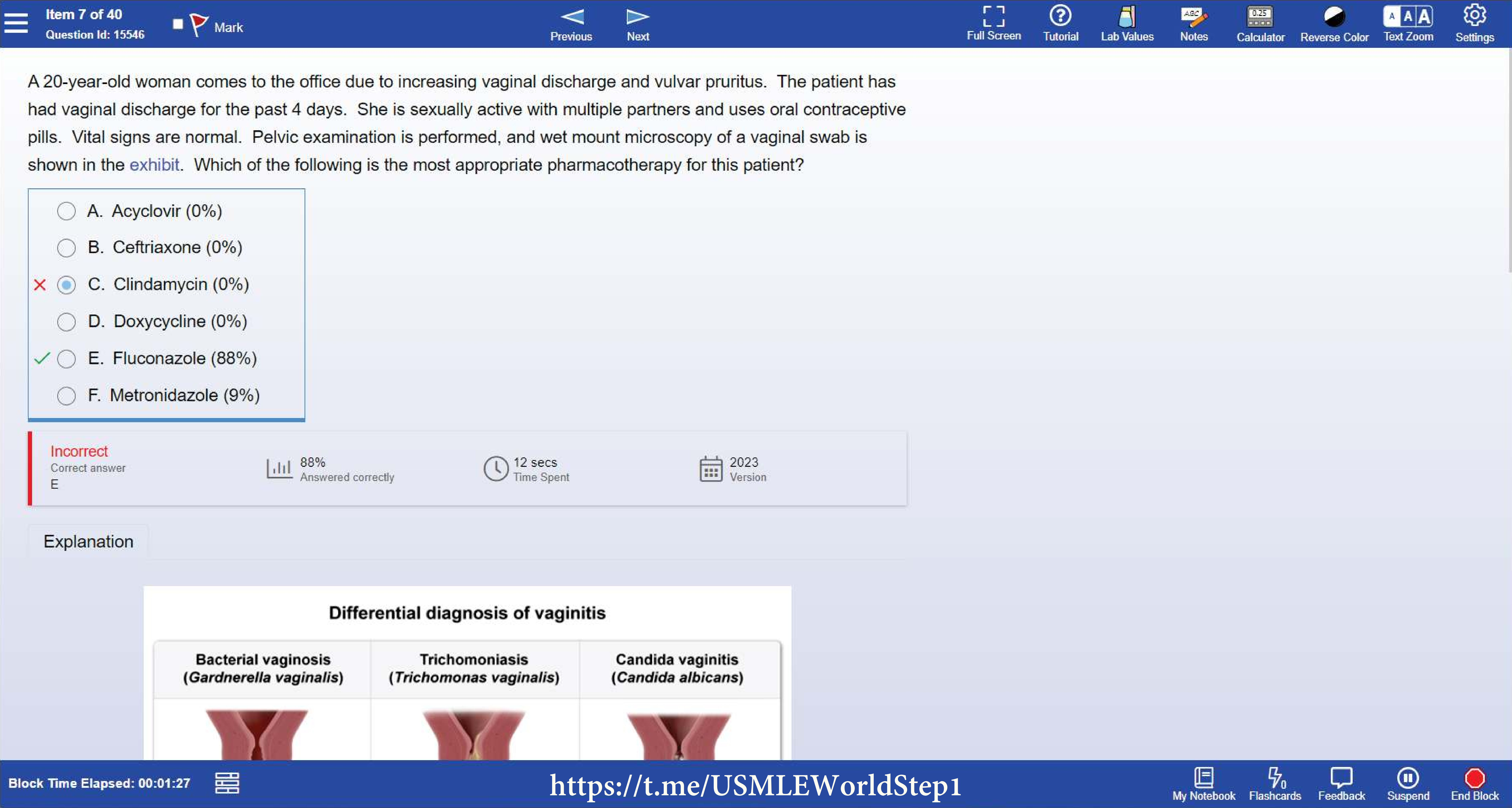
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A 20-year-old woman comes to the office due to increasing vaginal discharge and vulvar pruritus. The patient has had vaginal discharge for the past 4 days. She is sexually active with multiple partners and uses oral contraceptive pills. Vital signs are normal. Pelvic examination is performed, and wet mount microscopy of a vaginal swab is shown in the exhibit. Which of the following is the most appropriate pharmacotherapy for this patient?

- ○ A. Acyclovir (0%)
- ○ B. Ceftriaxone (0%)
- ✗ ● C. Clindamycin (0%)
- ○ D. Doxycycline (0%)
- ✓ ○ E. Fluconazole (88%)
- ○ F. Metronidazole (9%)

Incorrect
Correct answer
E

88%
Answered correctly

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Explanation

Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	**Trichomoniasis (*Trichomonas vaginalis*)**	**Candida vaginitis (*Candida albicans*)**

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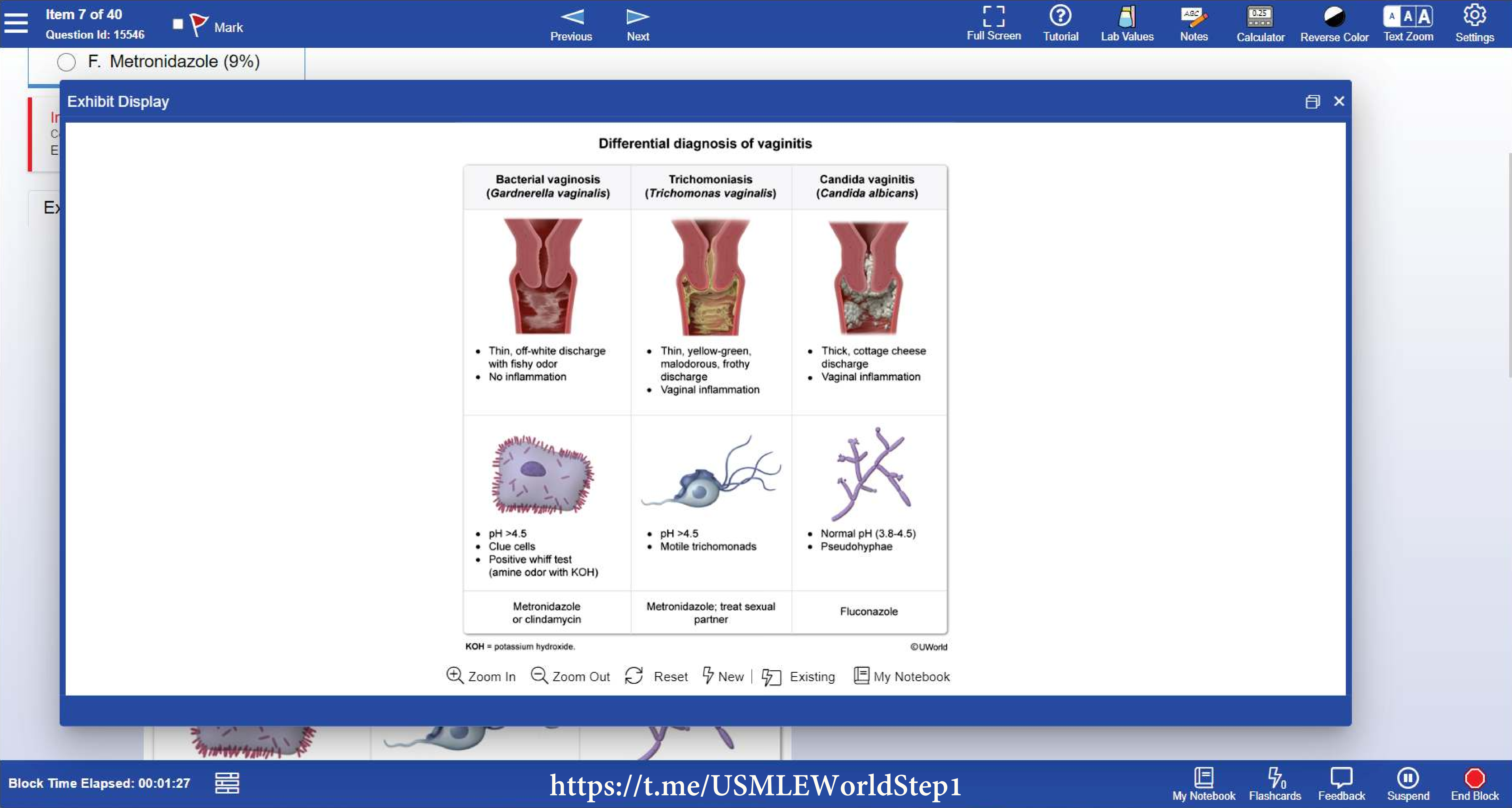
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○ F. Metronidazole (9%)

Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	Trichomoniasis (*Trichomonas vaginalis*)	Candida vaginitis (*Candida albicans*)
- Thin, off-white discharge with fishy odor - No inflammation	- Thin, yellow-green, malodorous, frothy discharge - Vaginal inflammation	- Thick, cottage cheese discharge - Vaginal inflammation
- pH >4.5 - Clue cells - Positive whiff test (amine odor with KOH)	- pH >4.5 - Motile trichomonads	- Normal pH (3.8-4.5) - Pseudohyphae
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

KOH = potassium hydroxide.

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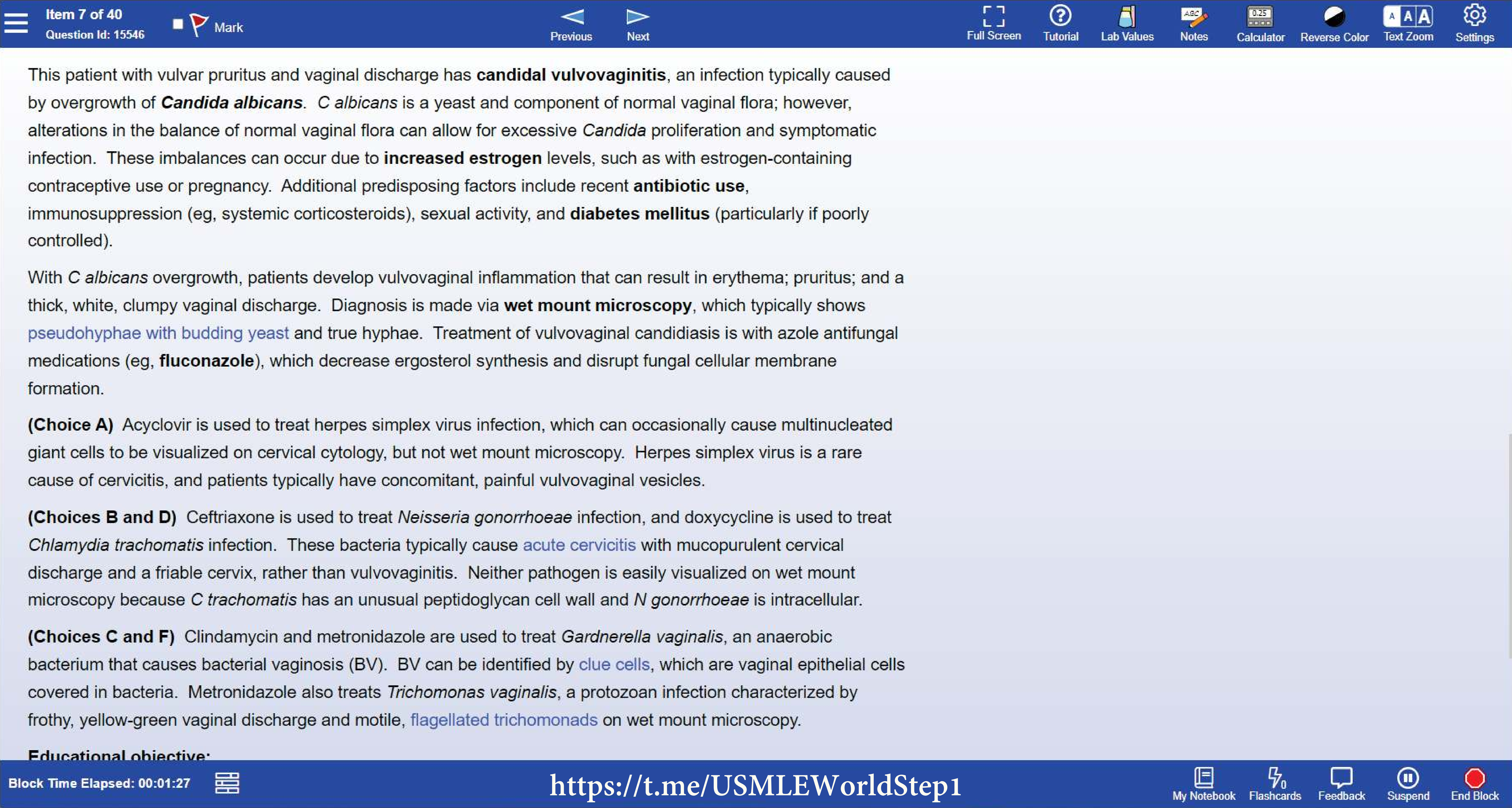


This patient with vulvar pruritus and vaginal discharge has **candidal vulvovaginitis**, an infection typically caused by overgrowth of ***Candida albicans***. *C albicans* is a yeast and component of normal vaginal flora; however, alterations in the balance of normal vaginal flora can allow for excessive *Candida* proliferation and symptomatic infection. These imbalances can occur due to **increased estrogen** levels, such as with estrogen-containing contraceptive use or pregnancy. Additional predisposing factors include recent **antibiotic use**, immunosuppression (eg, systemic corticosteroids), sexual activity, and **diabetes mellitus** (particularly if poorly controlled).

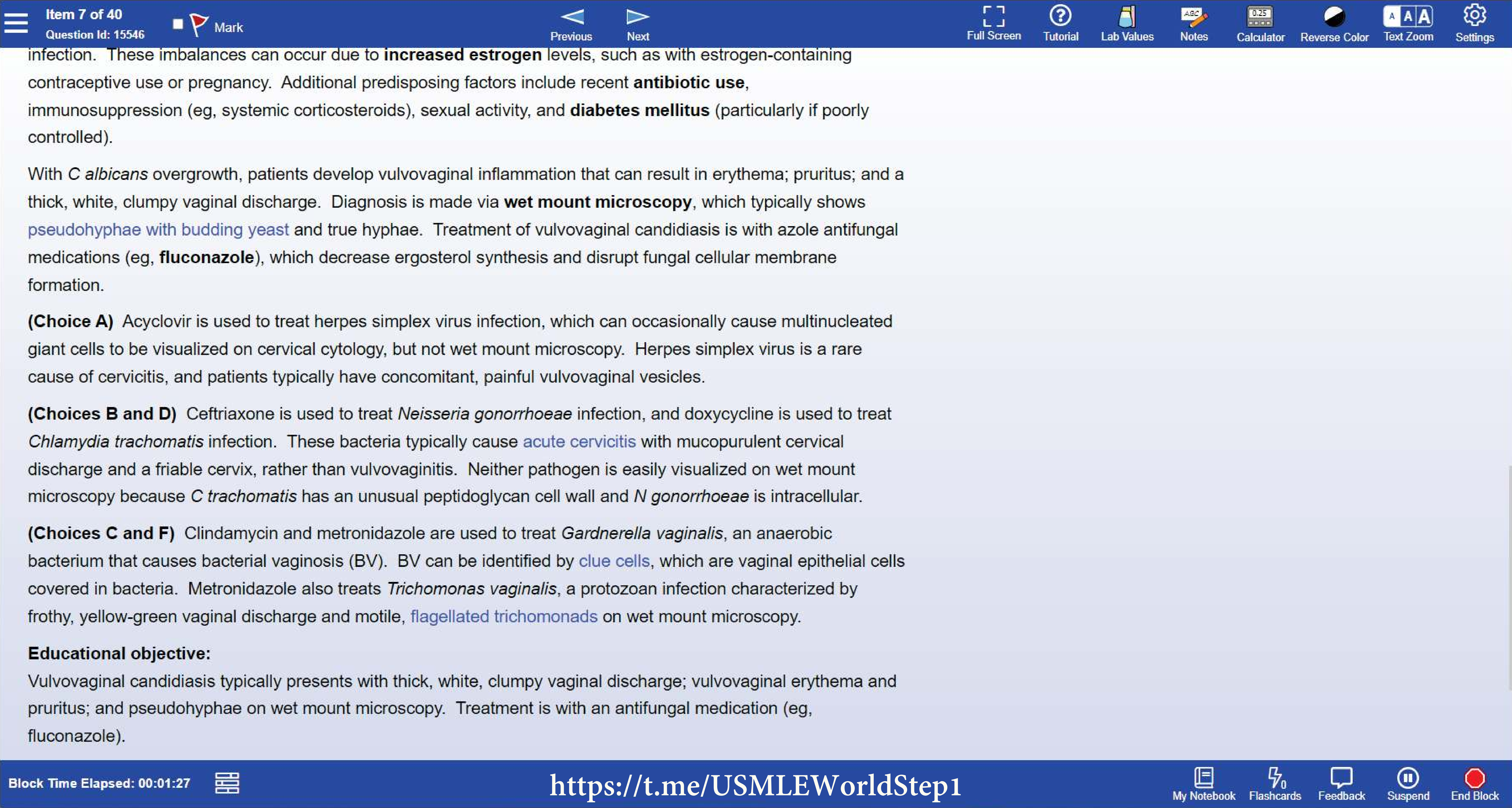
With *C albicans* overgrowth, patients develop vulvovaginal inflammation that can result in erythema; pruritus; and a thick, white, clumpy vaginal discharge. Diagnosis is made via **wet mount microscopy**, which typically shows pseudohyphae with budding yeast and true hyphae. Treatment of vulvovaginal candidiasis is with azole antifungal medications (eg, **fluconazole**), which decrease ergosterol synthesis and disrupt fungal cellular membrane formation.

(Choice A) Acyclovir is used to treat herpes simplex virus infection, which can occasionally cause multinucleated giant cells to be visualized on cervical cytology, but not wet mount microscopy. Herpes simplex virus is a rare cause of cervicitis, and patients typically have concomitant, painful vulvovaginal vesicles.

(Choices B and D) Ceftriaxone is used to treat *Neisseria gonorrhoeae* infection, and doxycycline is used to treat *Chlamydia trachomatis* infection. These bacteria typically cause acute cervicitis with mucopurulent cervical discharge and a friable cervix, rather than vulvovaginitis. Neither pathogen is easily visualized on wet mount microscopy because *C trachomatis* has an unusual peptidoglycan cell wall and *N gonorrhoeae* is intracellular.

(Choices C and F) Clindamycin and metronidazole are used to treat *Gardnerella vaginalis*, an anaerobic bacterium that causes bacterial vaginosis (BV). BV can be identified by clue cells, which are vaginal epithelial cells covered in bacteria. Metronidazole also treats *Trichomonas vaginalis*, a protozoan infection characterized by frothy, yellow-green vaginal discharge and motile, flagellated trichomonads on wet mount microscopy.

Educational objective:



infection. These imbalances can occur due to **increased estrogen** levels, such as with estrogen-containing contraceptive use or pregnancy. Additional predisposing factors include recent **antibiotic use**, immunosuppression (eg, systemic corticosteroids), sexual activity, and **diabetes mellitus** (particularly if poorly controlled).

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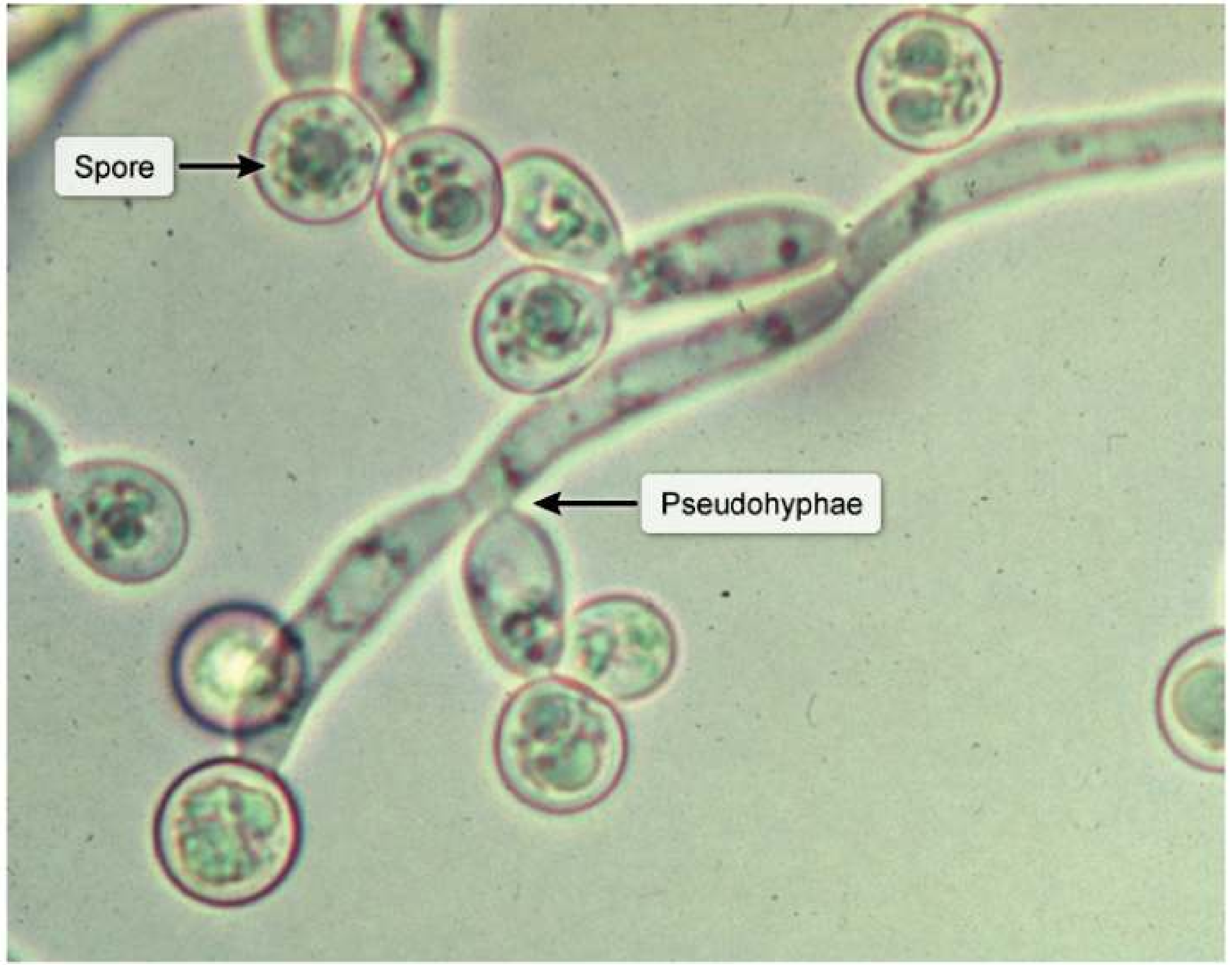
Educational objective:

Vulvovaginal candidiasis typically presents with thick, white, clumpy vaginal discharge; vulvovaginal erythema and pruritus; and pseudohyphae on wet mount microscopy. Treatment is with an antifungal medication (eg, fluconazole).

- Clue cells - Positive whiff test	- Motile trichomonads	- Pseudohyphae

Exhibit Display

Candida



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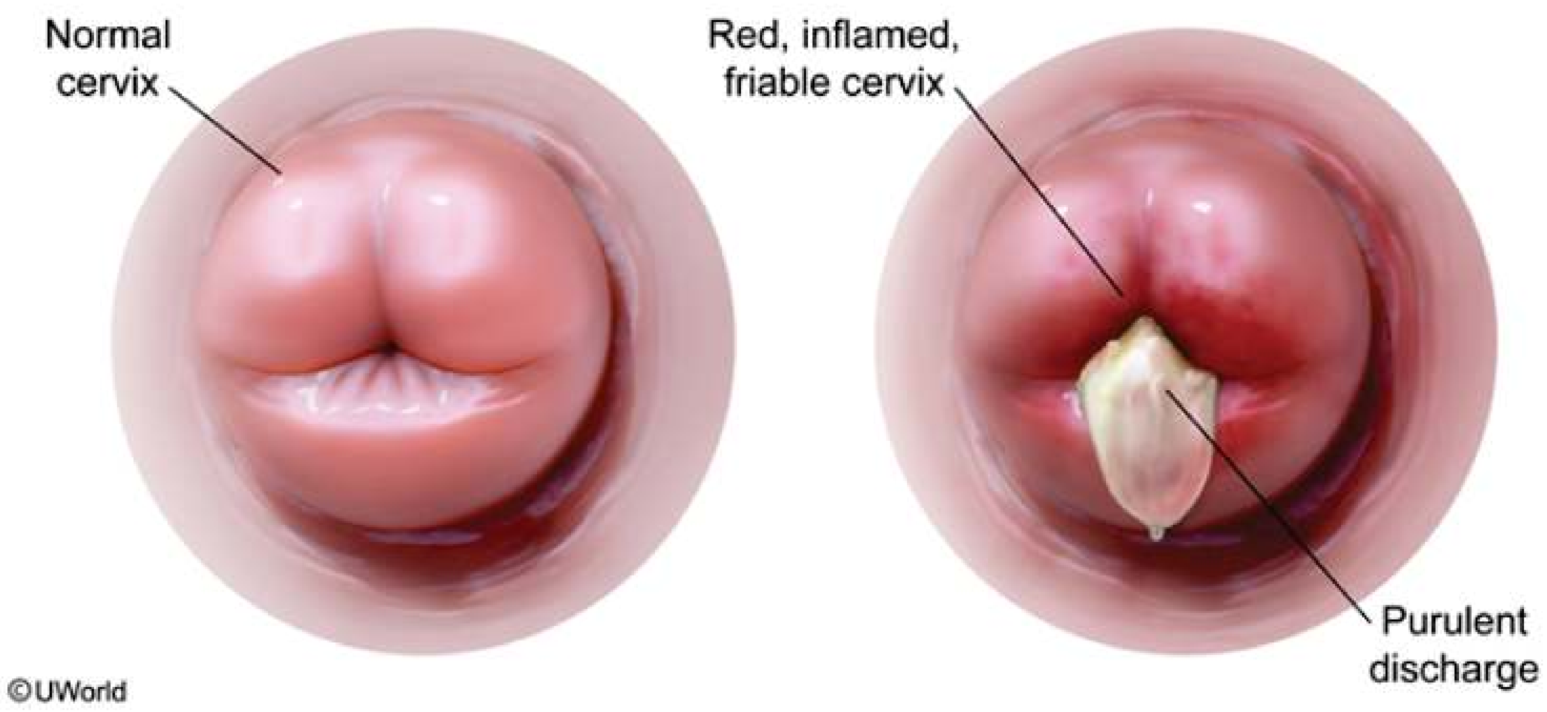
Cervicitis


Normal cervix
Red, inflamed, friable cervix
Purulent discharge
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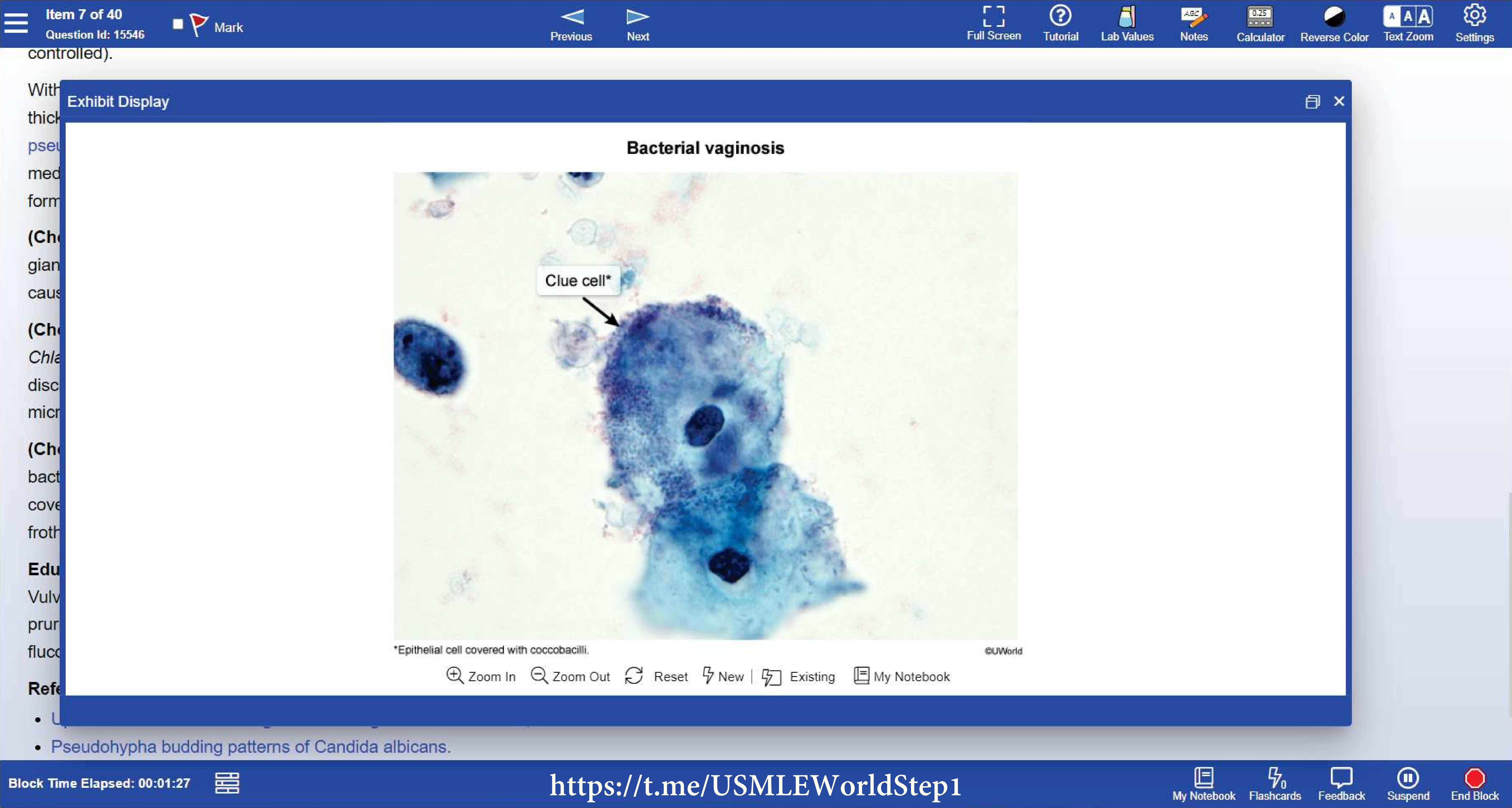
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- Pseudohypha budding patterns of Candida albicans.

Bacterial vaginosis

Clue cell*

*Epithelial cell covered with coccobacilli.

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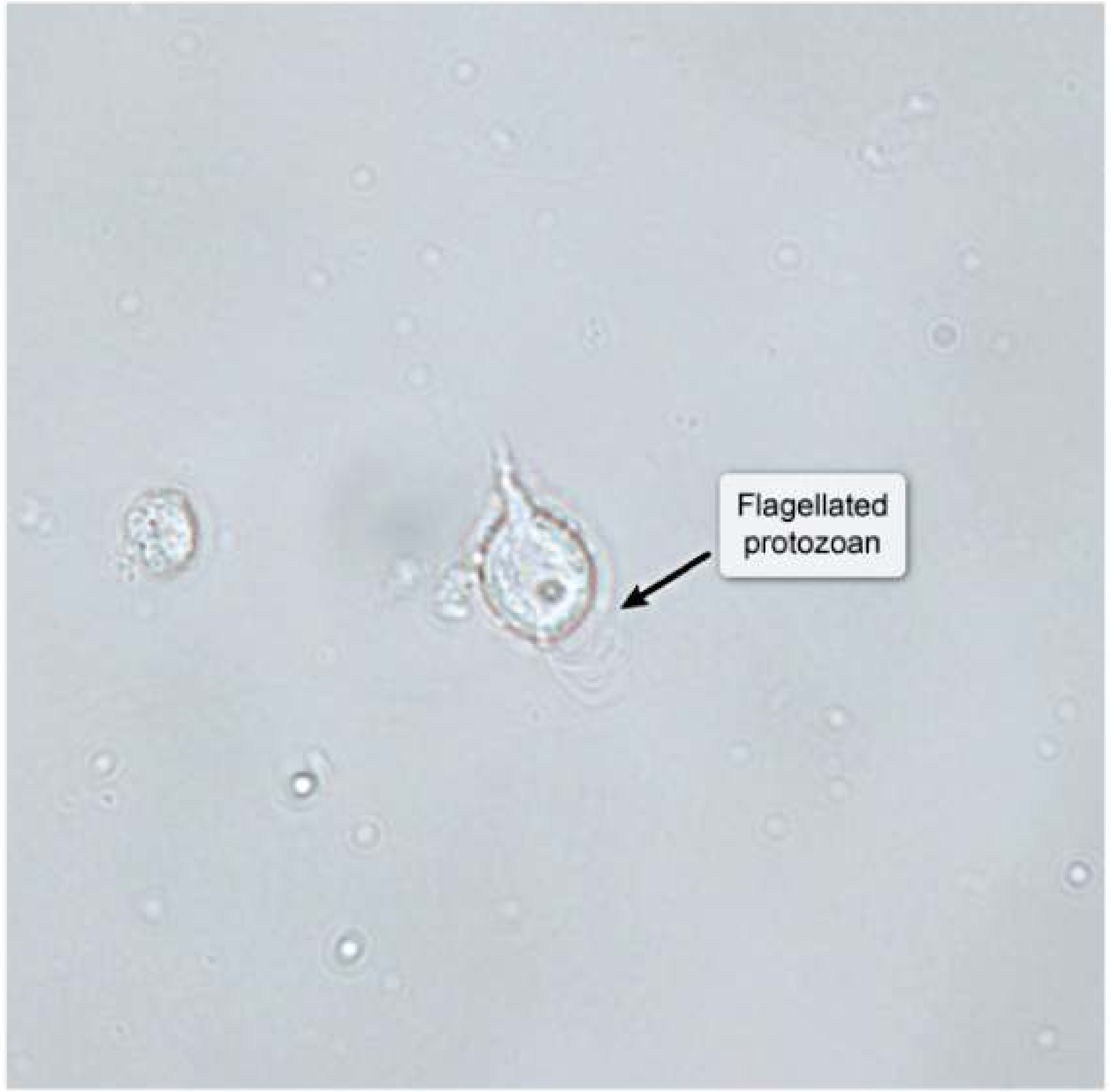
Exhibit Display

Trichomonas vaginalis


Flagellated protozoan

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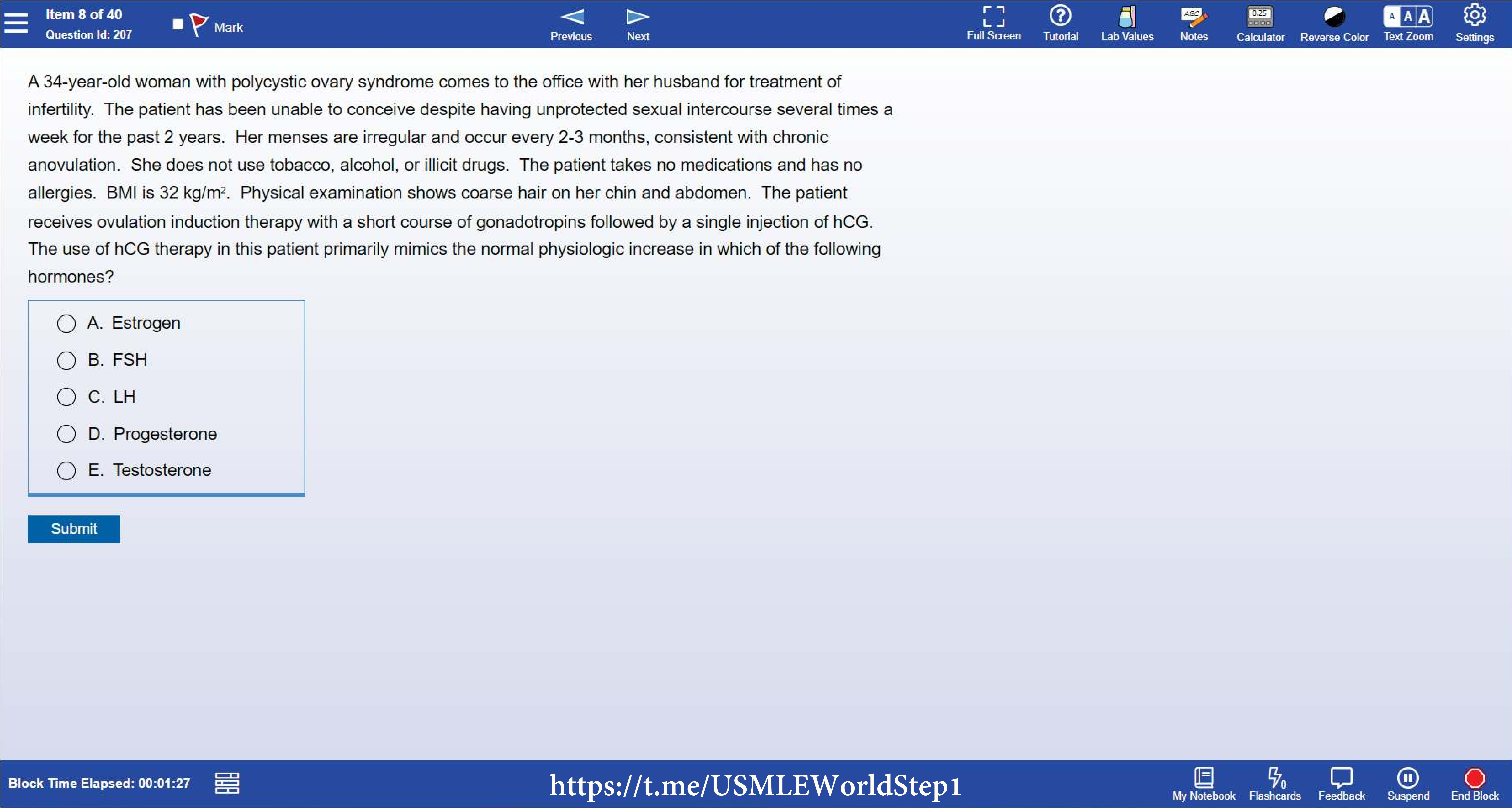
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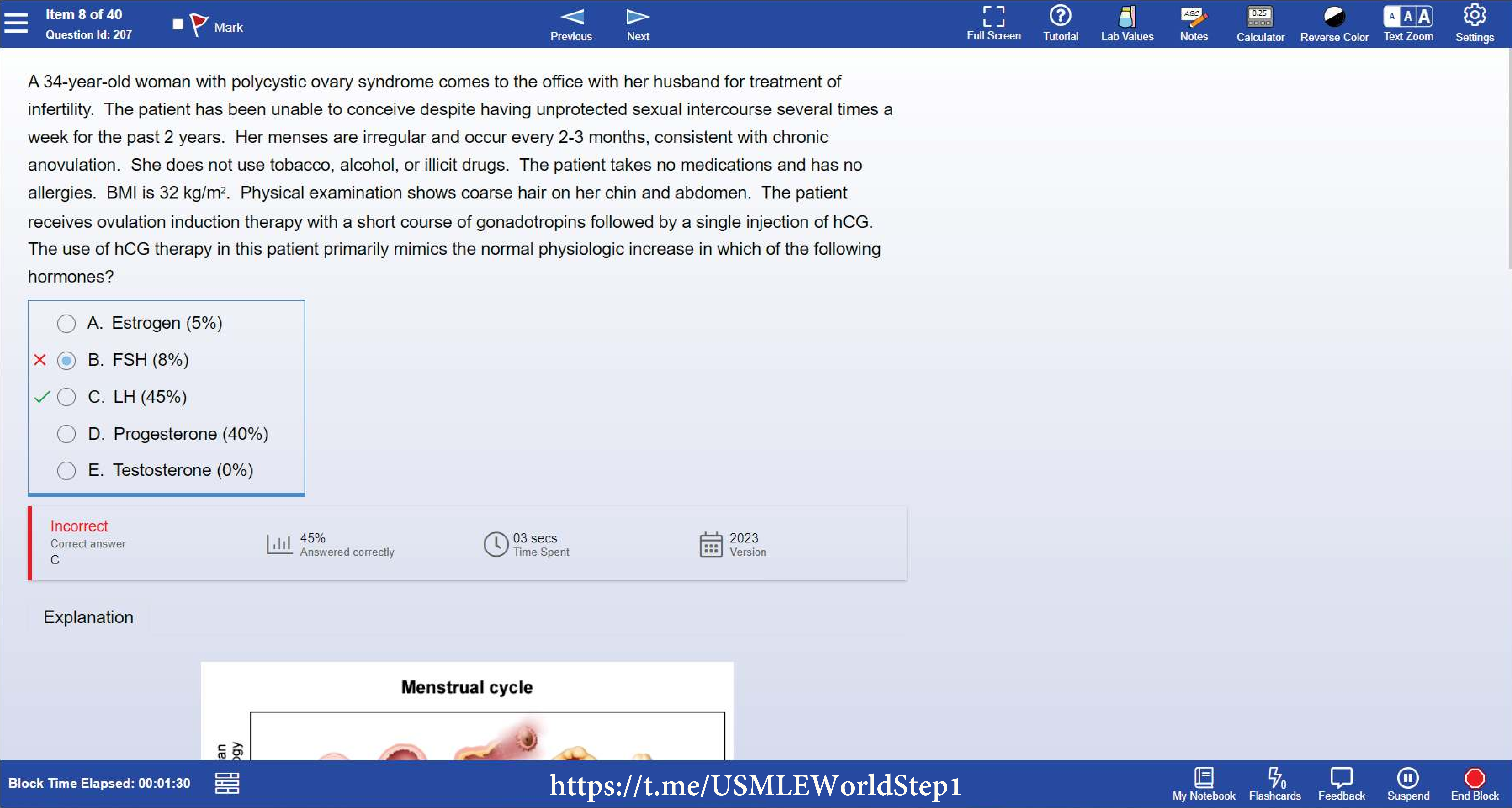
A 34-year-old woman with polycystic ovary syndrome comes to the office with her husband for treatment of infertility. The patient has been unable to conceive despite having unprotected sexual intercourse several times a week for the past 2 years. Her menses are irregular and occur every 2-3 months, consistent with chronic anovulation. She does not use tobacco, alcohol, or illicit drugs. The patient takes no medications and has no allergies. BMI is 32 kg/m^2. Physical examination shows coarse hair on her chin and abdomen. The patient receives ovulation induction therapy with a short course of gonadotropins followed by a single injection of hCG. The use of hCG therapy in this patient primarily mimics the normal physiologic increase in which of the following hormones?

○ A. Estrogen
○ B. FSH
○ C. LH
○ D. Progesterone
○ E. Testosterone

Submit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- ○ A. Estrogen (5%)
- ✗ ● B. FSH (8%)
- ✓ ○ C. LH (45%)
- ○ D. Progesterone (40%)
- ○ E. Testosterone (0%)

Incorrect
Correct answer
C

45%
Answered correctly

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Explanation

Menstrual cycle

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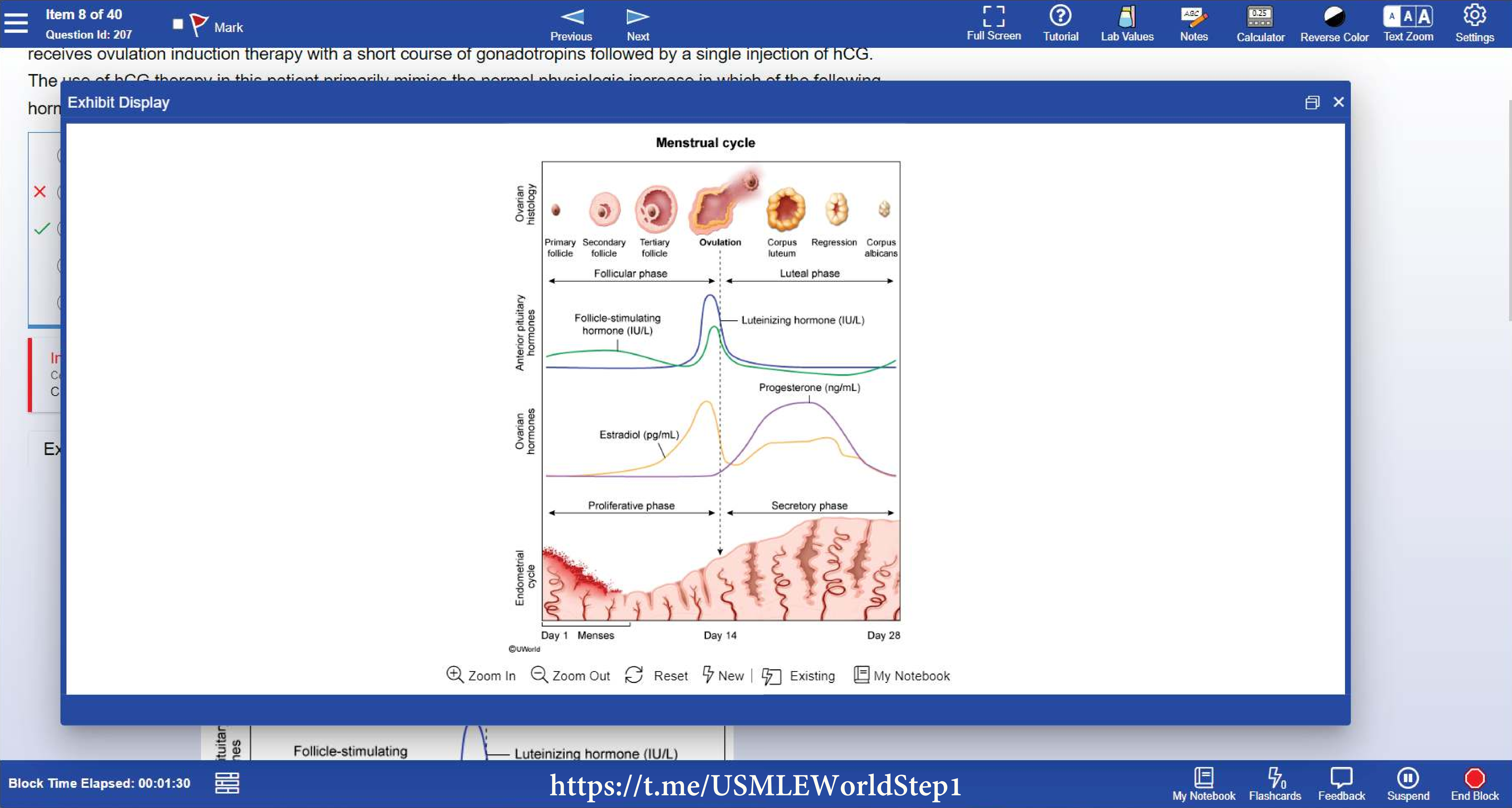
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Exhibit Display
Menstrual cycle
Ovarian histology
Primary follicle
Secondary follicle
Tertiary follicle
Ovulation
Corpus luteum
Regression
Corpus albicans
Follicular phase
Luteal phase
Anterior pituitary hormones
Follicle-stimulating hormone (IU/L)
Luteinizing hormone (IU/L)
Ovarian hormones
Progesterone (ng/mL)
Estradiol (pg/mL)
Proliferative phase
Secretory phase
Endometrial cycle
Day 1
Menses
Day 14
Day 28
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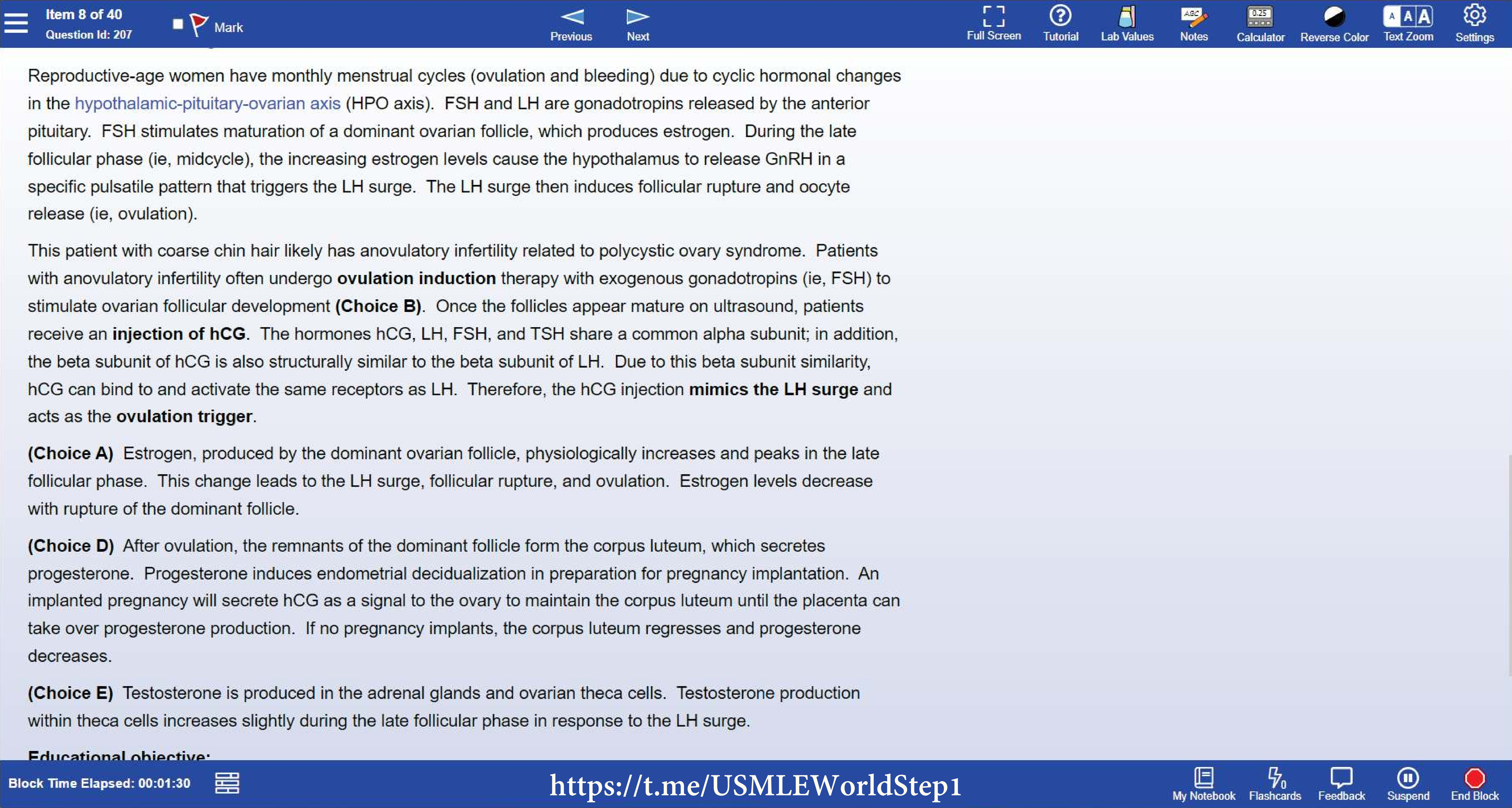
The use of hCG therapy in this patient primarily mimics the normal physiologic increase in which of the following horm



Reproductive-age women have monthly menstrual cycles (ovulation and bleeding) due to cyclic hormonal changes in the hypothalamic-pituitary-ovarian axis (HPO axis). FSH and LH are gonadotropins released by the anterior pituitary. FSH stimulates maturation of a dominant ovarian follicle, which produces estrogen. During the late follicular phase (ie, midcycle), the increasing estrogen levels cause the hypothalamus to release GnRH in a specific pulsatile pattern that triggers the LH surge. The LH surge then induces follicular rupture and oocyte release (ie, ovulation).

This patient with coarse chin hair likely has anovulatory infertility related to polycystic ovary syndrome. Patients with anovulatory infertility often undergo **ovulation induction** therapy with exogenous gonadotropins (ie, FSH) to stimulate ovarian follicular development **(Choice B)**. Once the follicles appear mature on ultrasound, patients receive an **injection of hCG**. The hormones hCG, LH, FSH, and TSH share a common alpha subunit; in addition, the beta subunit of hCG is also structurally similar to the beta subunit of LH. Due to this beta subunit similarity, hCG can bind to and activate the same receptors as LH. Therefore, the hCG injection **mimics the LH surge** and acts as the **ovulation trigger**.

(Choice A) Estrogen, produced by the dominant ovarian follicle, physiologically increases and peaks in the late follicular phase. This change leads to the LH surge, follicular rupture, and ovulation. Estrogen levels decrease with rupture of the dominant follicle.

(Choice D) After ovulation, the remnants of the dominant follicle form the corpus luteum, which secretes progesterone. Progesterone induces endometrial decidualization in preparation for pregnancy implantation. An implanted pregnancy will secrete hCG as a signal to the ovary to maintain the corpus luteum until the placenta can take over progesterone production. If no pregnancy implants, the corpus luteum regresses and progesterone decreases.

(Choice E) Testosterone is produced in the adrenal glands and ovarian theca cells. Testosterone production within theca cells increases slightly during the late follicular phase in response to the LH surge.

Educational objective:

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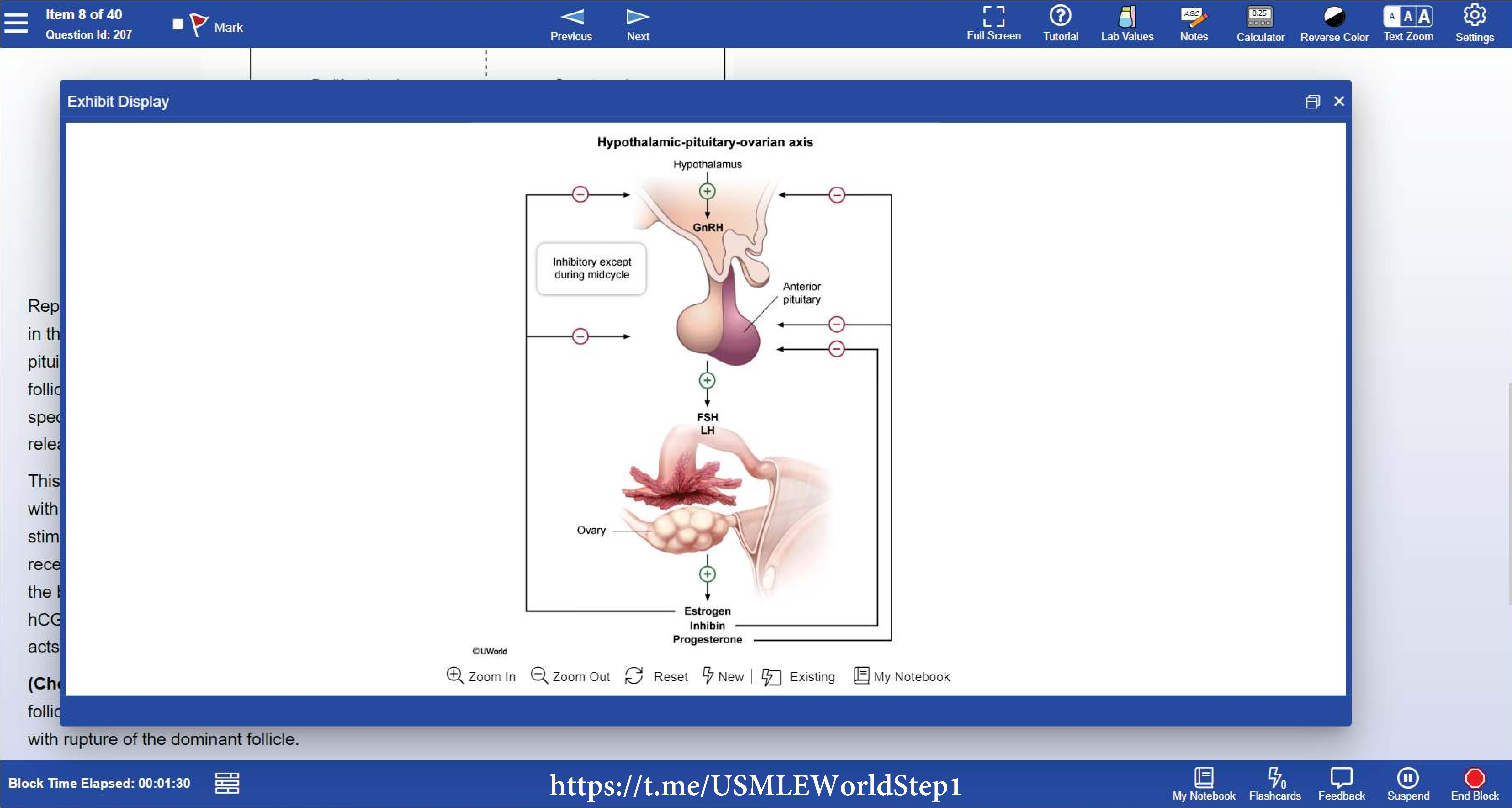
(Choice E) Testosterone is produced in the adrenal glands and ovarian theca cells. Testosterone production within theca cells increases slightly during the late follicular phase in response to the LH surge.

Educational objective:
Anovulatory infertility can be treated with ovulation induction therapy, which may include a course of gonadotropins to stimulate the ovarian follicles. Once the follicles mature, patients are administered an injection of hCG, which mimics the LH surge and acts as the ovulation trigger.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Hypothalamic-pituitary-ovarian axis

Hypothalamus
GnRH
Inhibitory except during midcycle
Anterior pituitary
FSH
LH
Ovary
Estrogen
Inhibin
Progesterone
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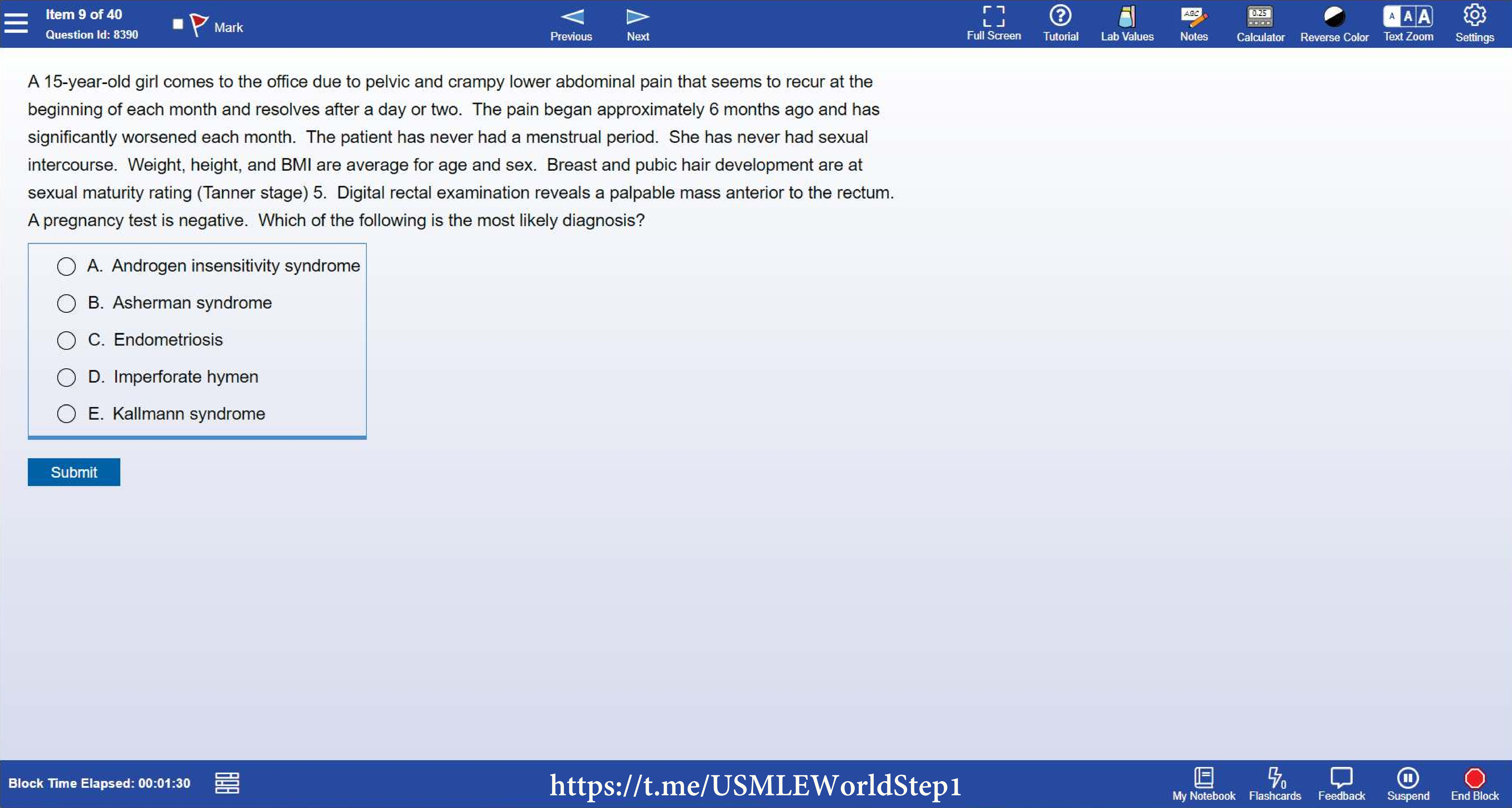
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Question Id: 8390

A 15-year-old girl comes to the office due to pelvic and crampy lower abdominal pain that seems to recur at the beginning of each month and resolves after a day or two. The pain began approximately 6 months ago and has significantly worsened each month. The patient has never had a menstrual period. She has never had sexual intercourse. Weight, height, and BMI are average for age and sex. Breast and pubic hair development are at sexual maturity rating (Tanner stage) 5. Digital rectal examination reveals a palpable mass anterior to the rectum. A pregnancy test is negative. Which of the following is the most likely diagnosis?

- ○ A. Androgen insensitivity syndrome
- ○ B. Asherman syndrome
- ○ C. Endometriosis
- ○ D. Imperforate hymen
- ○ E. Kallmann syndrome

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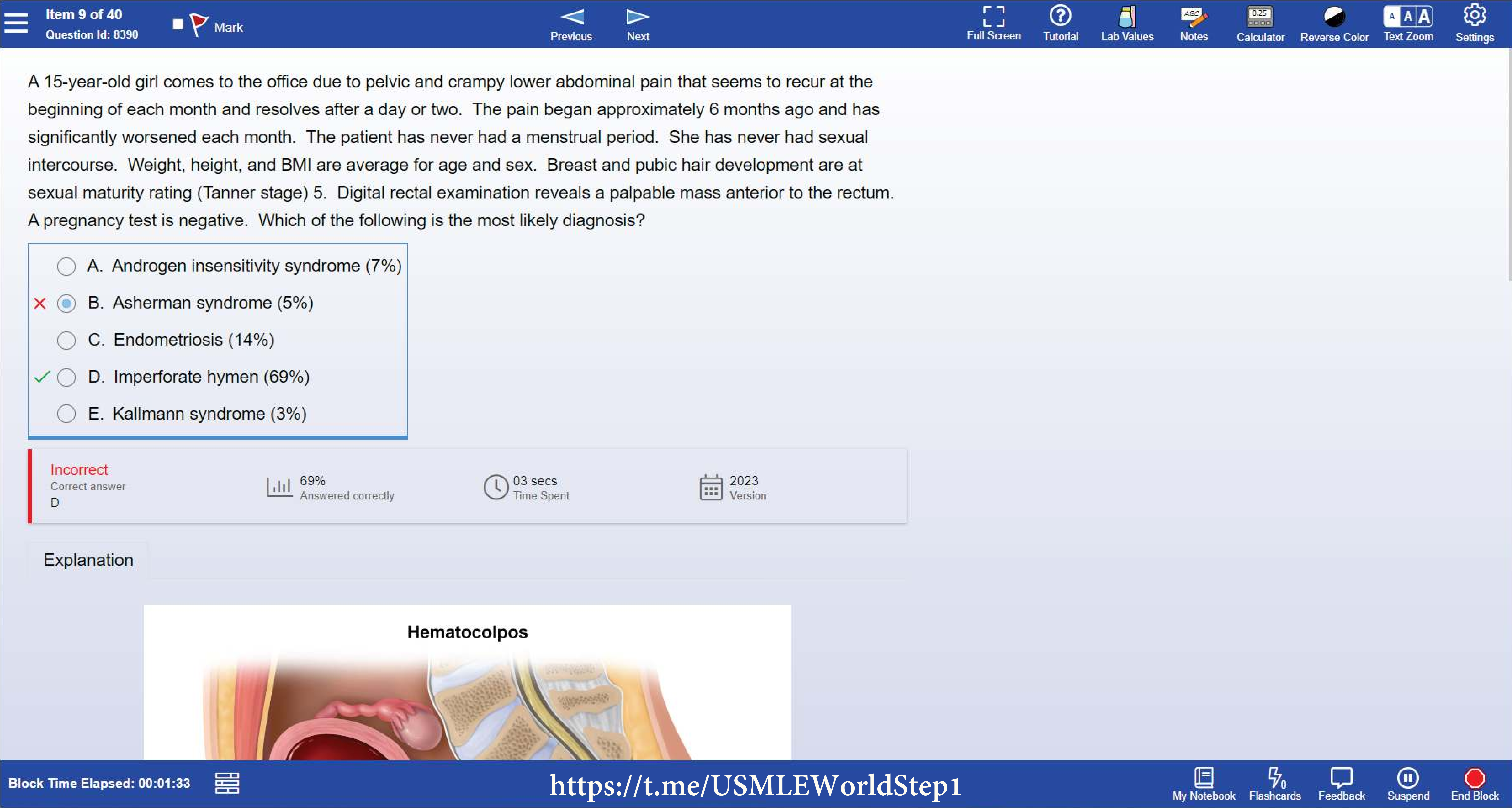
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- ○ A. Androgen insensitivity syndrome (7%)
- ✗ ● B. Asherman syndrome (5%)
- ○ C. Endometriosis (14%)
- ✓ ○ D. Imperforate hymen (69%)
- ○ E. Kallmann syndrome (3%)

Incorrect
Correct answer
D

69%
Answered correctly

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Explanation

Hematocolpos

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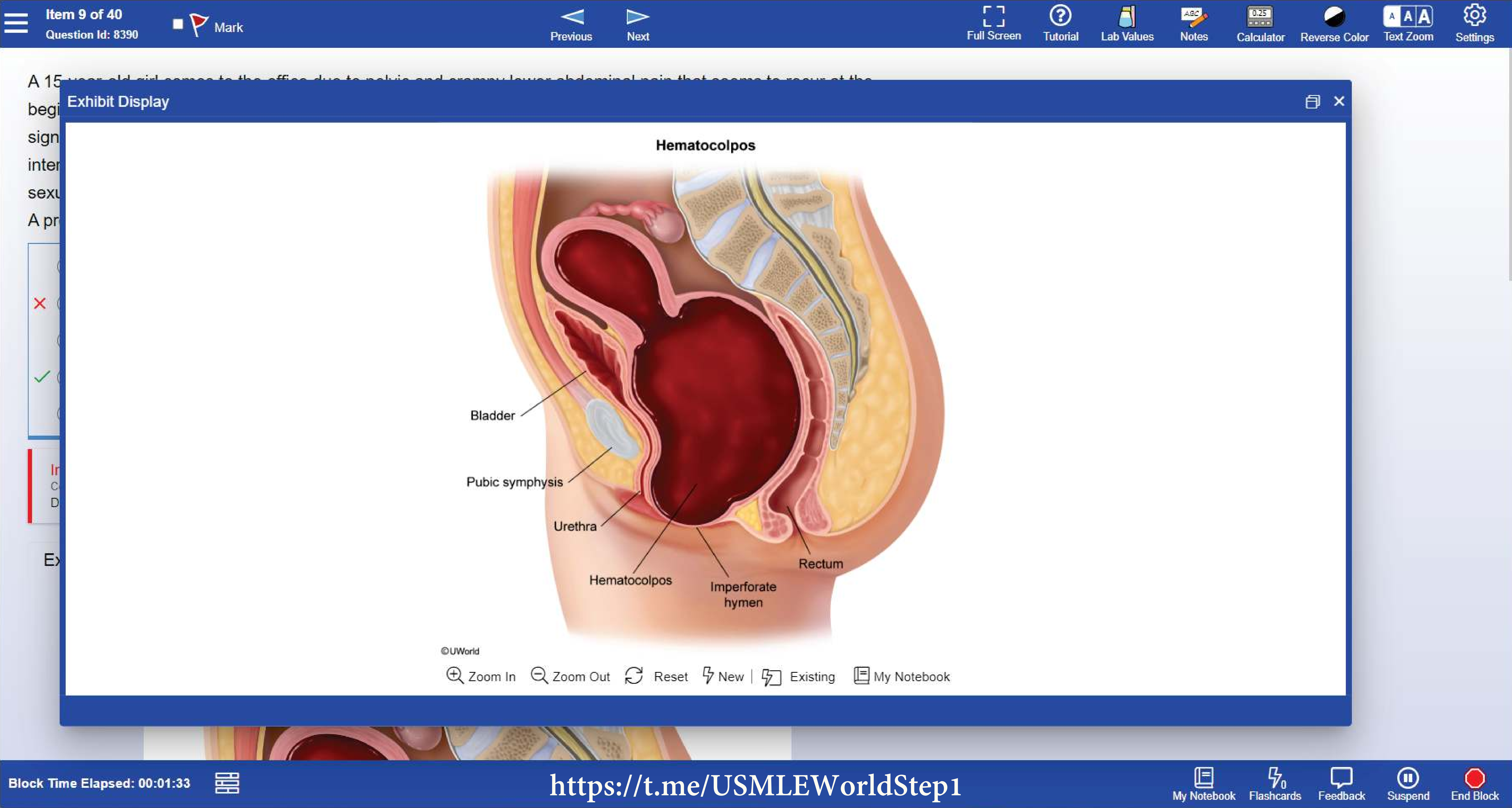

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Question Id: 8390

A 15 year old girl comes to the office due to pelvic and crampy lower abdominal pain that seems to recur at the
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Exhibit Display

Hematocolpos

Bladder
Pubic symphysis
Urethra
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Imperforate hymen
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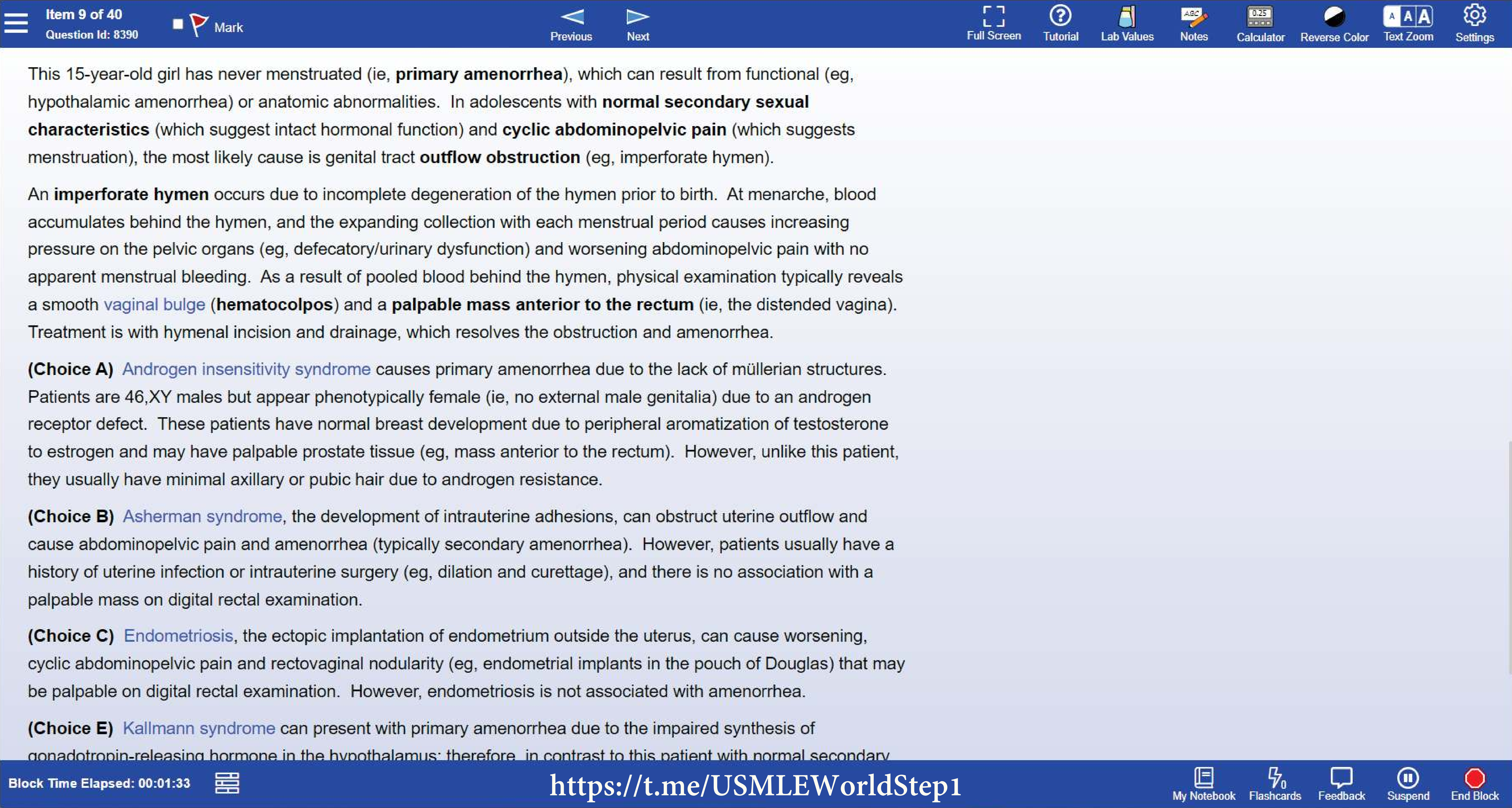


This 15-year-old girl has never menstruated (ie, **primary amenorrhea**), which can result from functional (eg, hypothalamic amenorrhea) or anatomic abnormalities. In adolescents with **normal secondary sexual characteristics** (which suggest intact hormonal function) and **cyclic abdominopelvic pain** (which suggests menstruation), the most likely cause is genital tract **outflow obstruction** (eg, imperforate hymen).

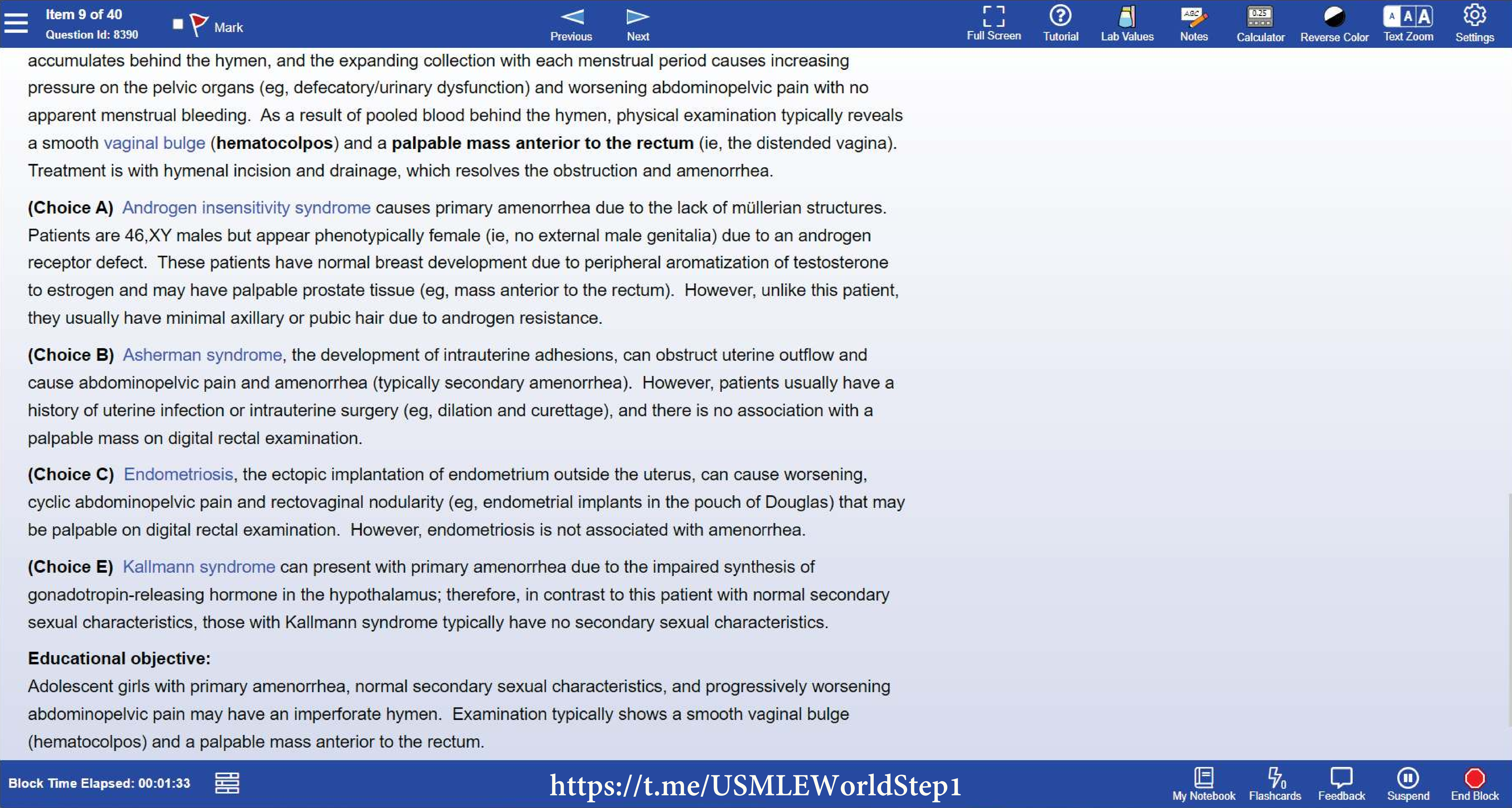
An **imperforate hymen** occurs due to incomplete degeneration of the hymen prior to birth. At menarche, blood accumulates behind the hymen, and the expanding collection with each menstrual period causes increasing pressure on the pelvic organs (eg, defecatory/urinary dysfunction) and worsening abdominopelvic pain with no apparent menstrual bleeding. As a result of pooled blood behind the hymen, physical examination typically reveals a smooth vaginal bulge (**hematocolpos**) and a **palpable mass anterior to the rectum** (ie, the distended vagina). Treatment is with hymenal incision and drainage, which resolves the obstruction and amenorrhea.

(Choice A) Androgen insensitivity syndrome causes primary amenorrhea due to the lack of müllerian structures. Patients are 46,XY males but appear phenotypically female (ie, no external male genitalia) due to an androgen receptor defect. These patients have normal breast development due to peripheral aromatization of testosterone to estrogen and may have palpable prostate tissue (eg, mass anterior to the rectum). However, unlike this patient, they usually have minimal axillary or pubic hair due to androgen resistance.

(Choice B) Asherman syndrome, the development of intrauterine adhesions, can obstruct uterine outflow and cause abdominopelvic pain and amenorrhea (typically secondary amenorrhea). However, patients usually have a history of uterine infection or intrauterine surgery (eg, dilation and curettage), and there is no association with a palpable mass on digital rectal examination.

(Choice C) Endometriosis, the ectopic implantation of endometrium outside the uterus, can cause worsening, cyclic abdominopelvic pain and rectovaginal nodularity (eg, endometrial implants in the pouch of Douglas) that may be palpable on digital rectal examination. However, endometriosis is not associated with amenorrhea.

(Choice E) Kallmann syndrome can present with primary amenorrhea due to the impaired synthesis of gonadotropin-releasing hormone in the hypothalamus; therefore, in contrast to this patient with normal secondary



accumulates behind the hymen, and the expanding collection with each menstrual period causes increasing pressure on the pelvic organs (eg, defecatory/urinary dysfunction) and worsening abdominopelvic pain with no apparent menstrual bleeding. As a result of pooled blood behind the hymen, physical examination typically reveals a smooth vaginal bulge (**hematocolpos**) and a **palpable mass anterior to the rectum** (ie, the distended vagina). Treatment is with hymenal incision and drainage, which resolves the obstruction and amenorrhea.

(Choice A) Androgen insensitivity syndrome causes primary amenorrhea due to the lack of müllerian structures. Patients are 46,XY males but appear phenotypically female (ie, no external male genitalia) due to an androgen receptor defect. These patients have normal breast development due to peripheral aromatization of testosterone to estrogen and may have palpable prostate tissue (eg, mass anterior to the rectum). However, unlike this patient, they usually have minimal axillary or pubic hair due to androgen resistance.

(Choice B) Asherman syndrome, the development of intrauterine adhesions, can obstruct uterine outflow and cause abdominopelvic pain and amenorrhea (typically secondary amenorrhea). However, patients usually have a history of uterine infection or intrauterine surgery (eg, dilation and curettage), and there is no association with a palpable mass on digital rectal examination.

(Choice C) Endometriosis, the ectopic implantation of endometrium outside the uterus, can cause worsening, cyclic abdominopelvic pain and rectovaginal nodularity (eg, endometrial implants in the pouch of Douglas) that may be palpable on digital rectal examination. However, endometriosis is not associated with amenorrhea.

(Choice E) Kallmann syndrome can present with primary amenorrhea due to the impaired synthesis of gonadotropin-releasing hormone in the hypothalamus; therefore, in contrast to this patient with normal secondary sexual characteristics, those with Kallmann syndrome typically have no secondary sexual characteristics.

Educational objective:

Adolescent girls with primary amenorrhea, normal secondary sexual characteristics, and progressively worsening abdominopelvic pain may have an imperforate hymen. Examination typically shows a smooth vaginal bulge (hematocolpos) and a palpable mass anterior to the rectum.

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This 15-year-old girl has never menstruated (ie, **primary amenorrhea**), which can result from functional (eg,

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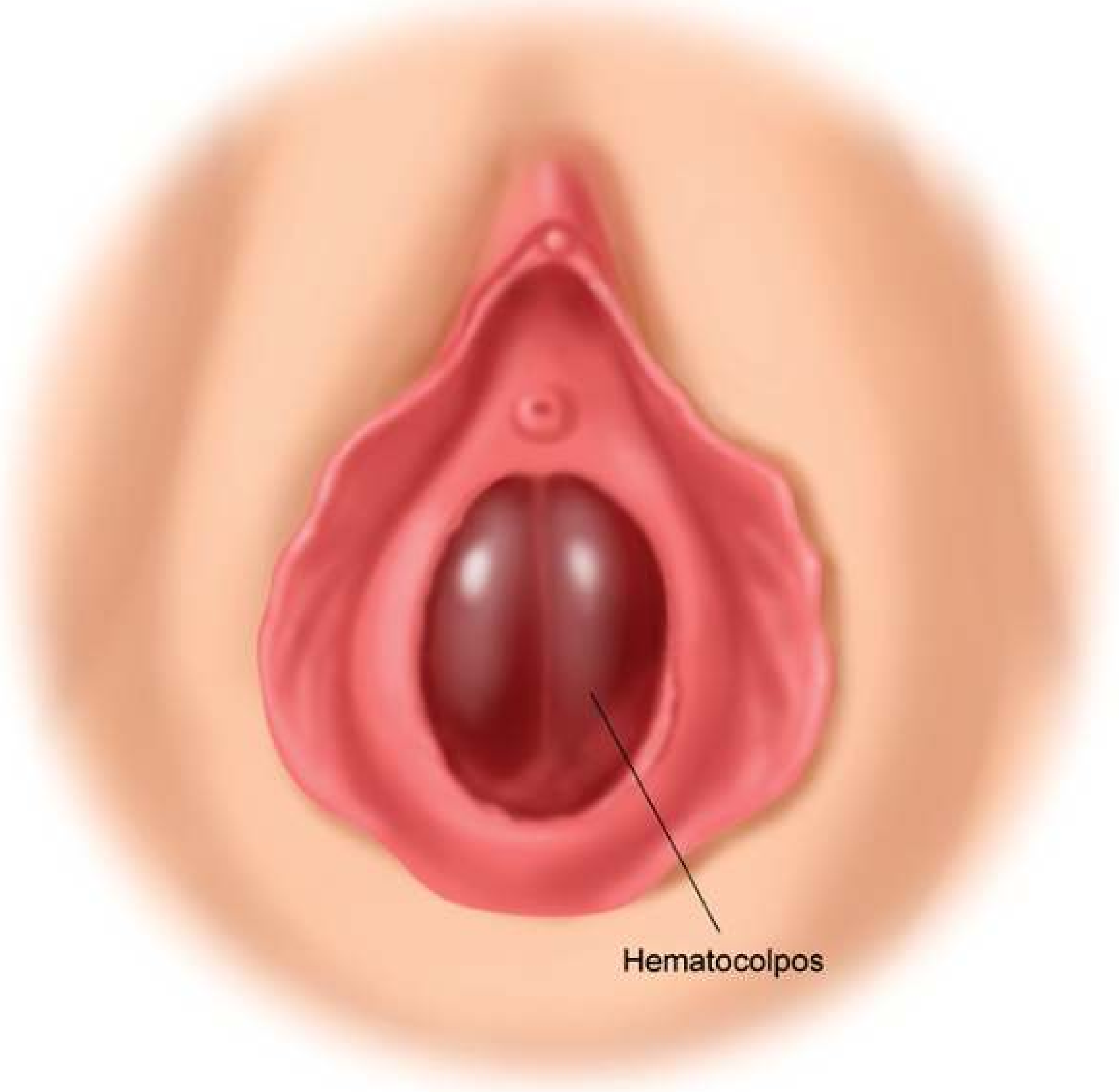
Imperforate hymen



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(Choice E) Kallmann syndrome can present with primary amenorrhea due to the impaired synthesis of

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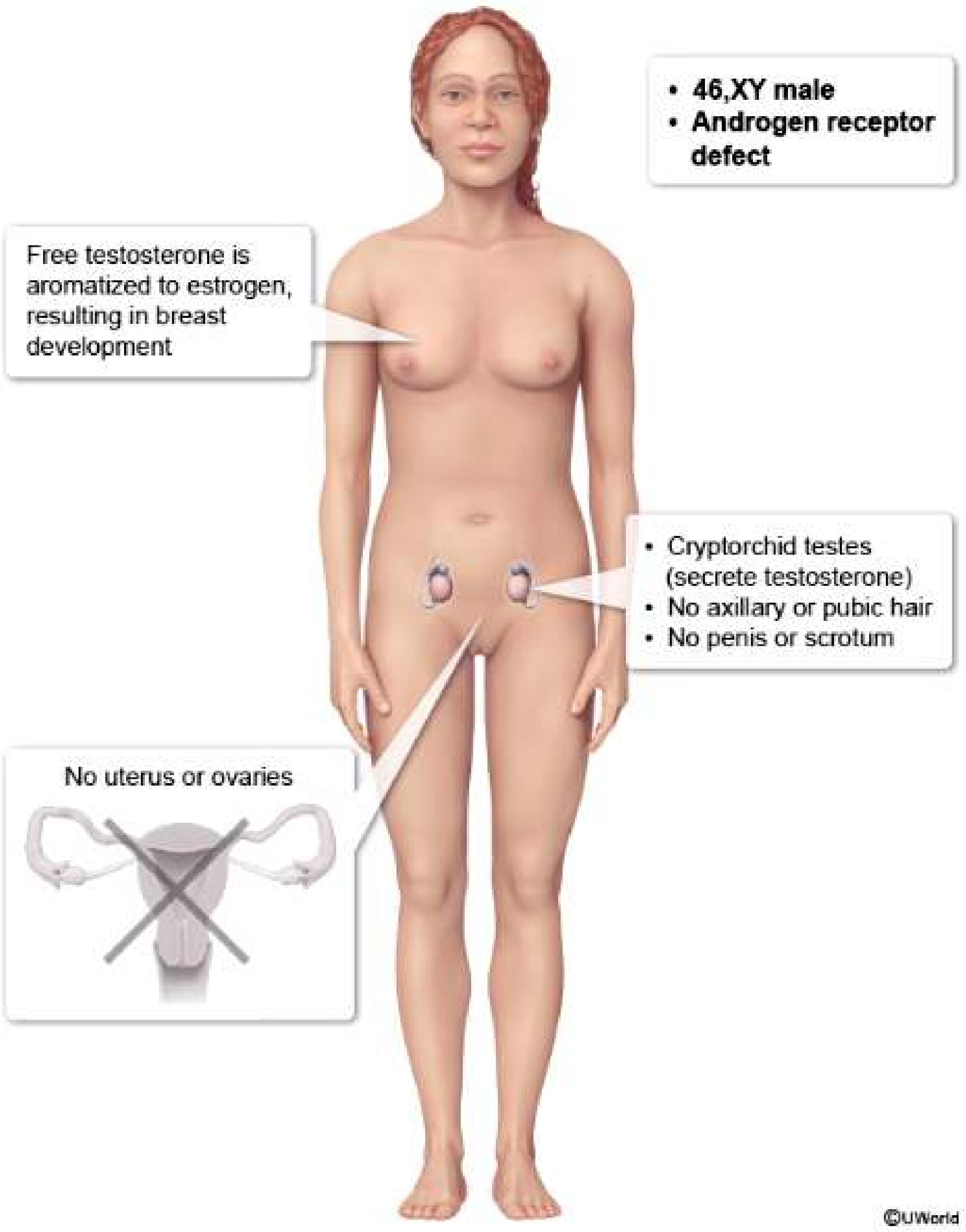
Androgen insensitivity syndrome



- **46,XY male**
- **Androgen receptor defect**

Free testosterone is aromatized to estrogen, resulting in breast development

- Cryptorchid testes (secrete testosterone)
- No axillary or pubic hair
- No penis or scrotum

No uterus or ovaries

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(Choice E) Kallmann syndrome can present with primary amenorrhea due to the impaired synthesis of

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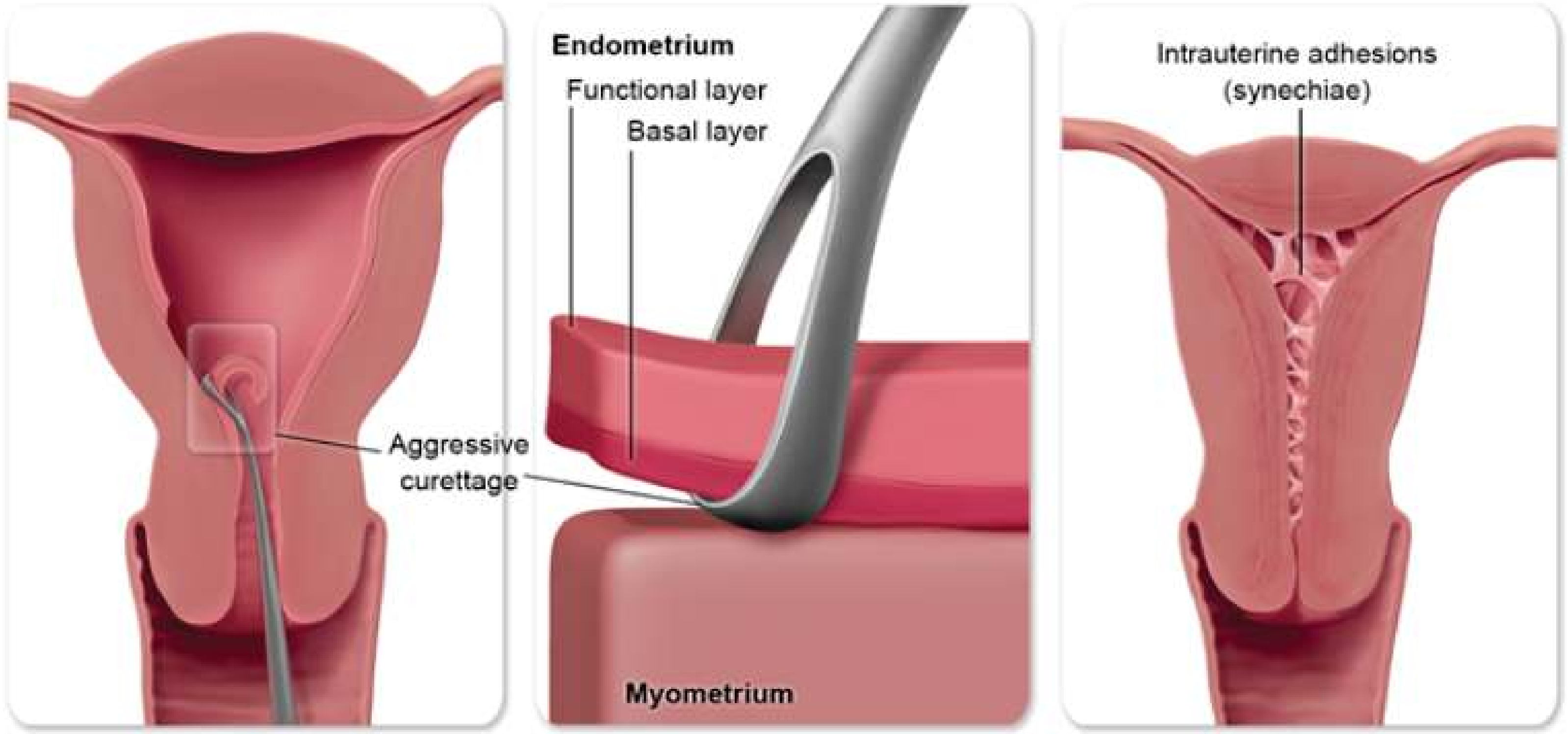
Asherman syndrome


Endometrium
Functional layer
Basal layer
Aggressive curettage
Myometrium
Intrauterine adhesions (synechiae)

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(Choice E) Kallmann syndrome can present with primary amenorrhea due to the impaired synthesis of

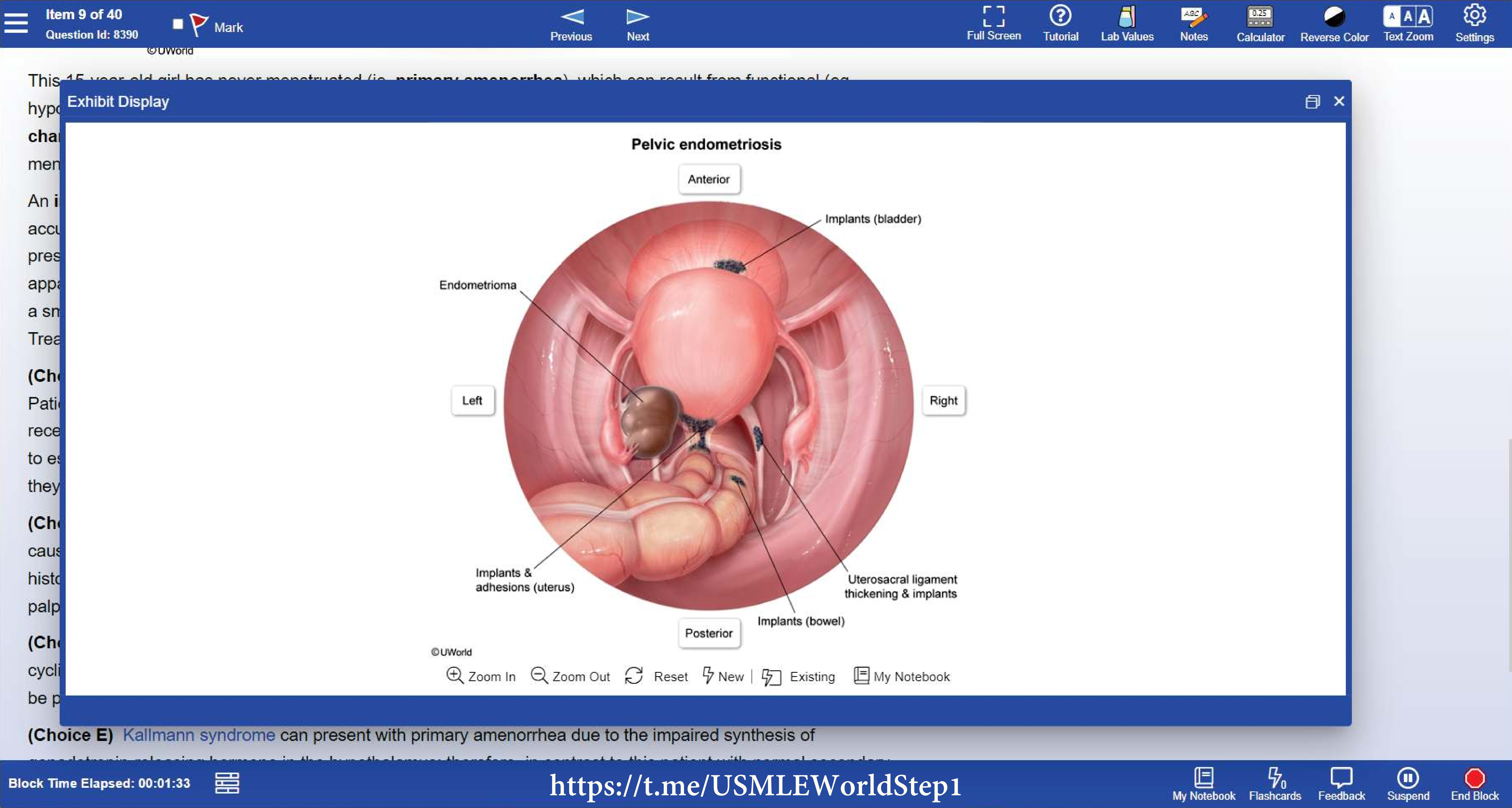
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Exhibit Display
Pelvic endometriosis
Anterior
Implants (bladder)
Endometrioma
Left
Right
Implants & adhesions (uterus)
Uterosacral ligament thickening & implants
Implants (bowel)
Posterior
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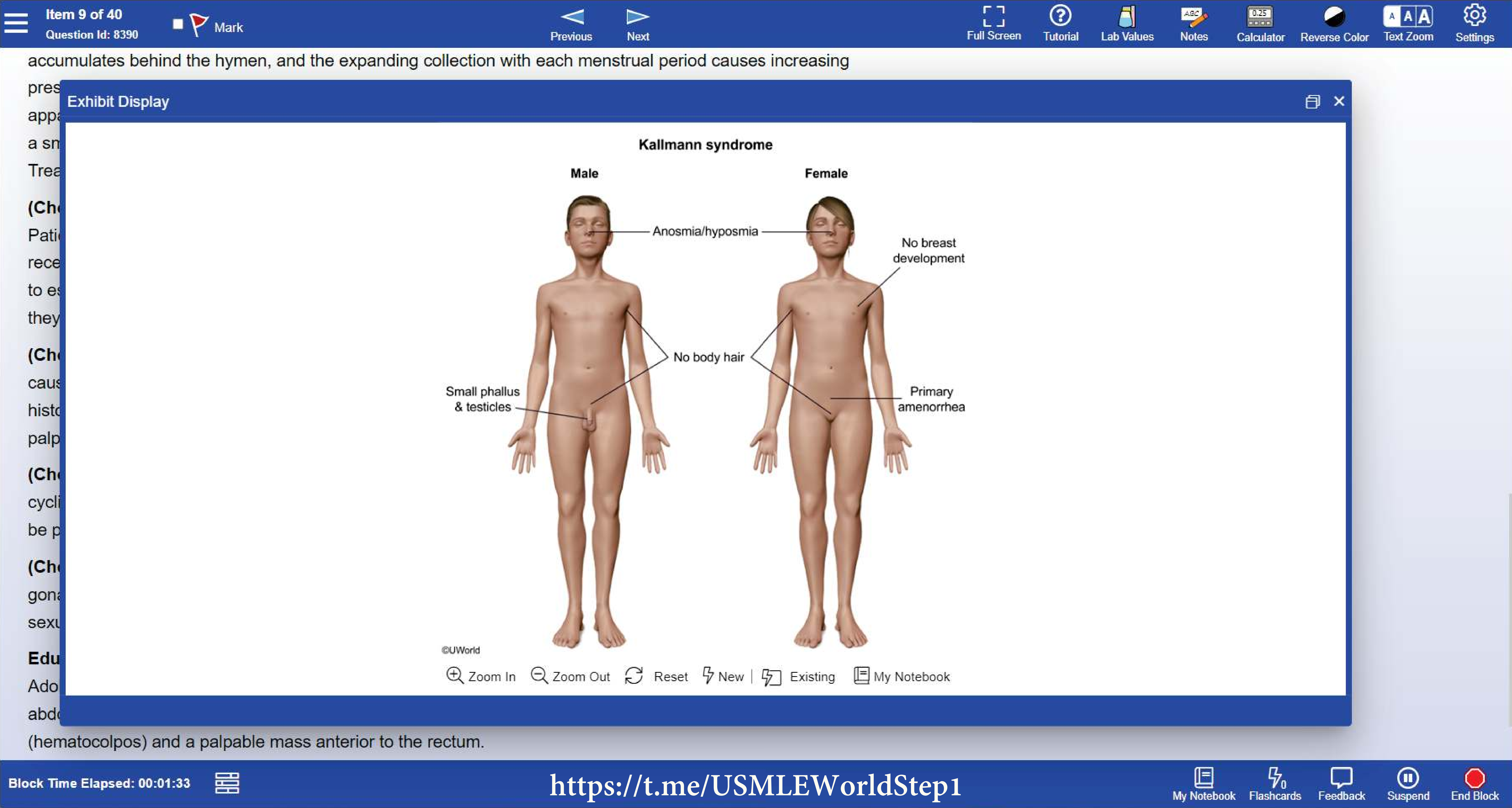
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accumulates behind the hymen, and the expanding collection with each menstrual period causes increasing

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(hematocolpos) and a palpable mass anterior to the rectum.

Exhibit Display

Kallmann syndrome

Male
Female
Anosmia/hyposmia
No breast development
No body hair
Small phallus & testicles
Primary amenorrhea
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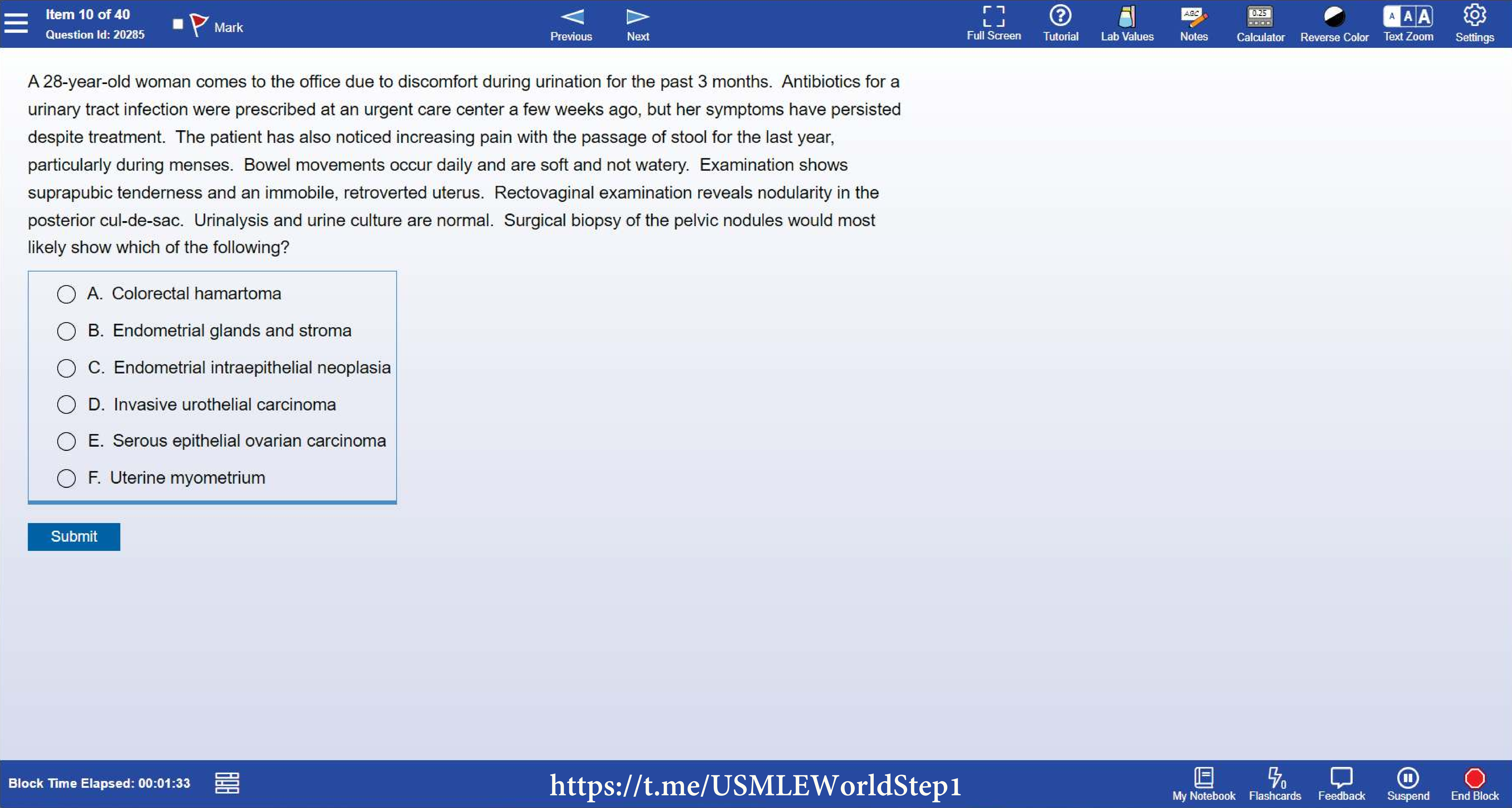
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A 28-year-old woman comes to the office due to discomfort during urination for the past 3 months. Antibiotics for a urinary tract infection were prescribed at an urgent care center a few weeks ago, but her symptoms have persisted despite treatment. The patient has also noticed increasing pain with the passage of stool for the last year, particularly during menses. Bowel movements occur daily and are soft and not watery. Examination shows suprapubic tenderness and an immobile, retroverted uterus. Rectovaginal examination reveals nodularity in the posterior cul-de-sac. Urinalysis and urine culture are normal. Surgical biopsy of the pelvic nodules would most likely show which of the following?

○ A. Colorectal hamartoma
○ B. Endometrial glands and stroma
○ C. Endometrial intraepithelial neoplasia
○ D. Invasive urothelial carcinoma
○ E. Serous epithelial ovarian carcinoma
○ F. Uterine myometrium

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- ○ A. Colorectal hamartoma (2%)
- ✓ ● B. Endometrial glands and stroma (75%)
- ○ C. Endometrial intraepithelial neoplasia (4%)
- ○ D. Invasive urothelial carcinoma (2%)
- ○ E. Serous epithelial ovarian carcinoma (2%)
- ○ F. Uterine myometrium (11%)

Correct

75%
Answered correctly

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Version

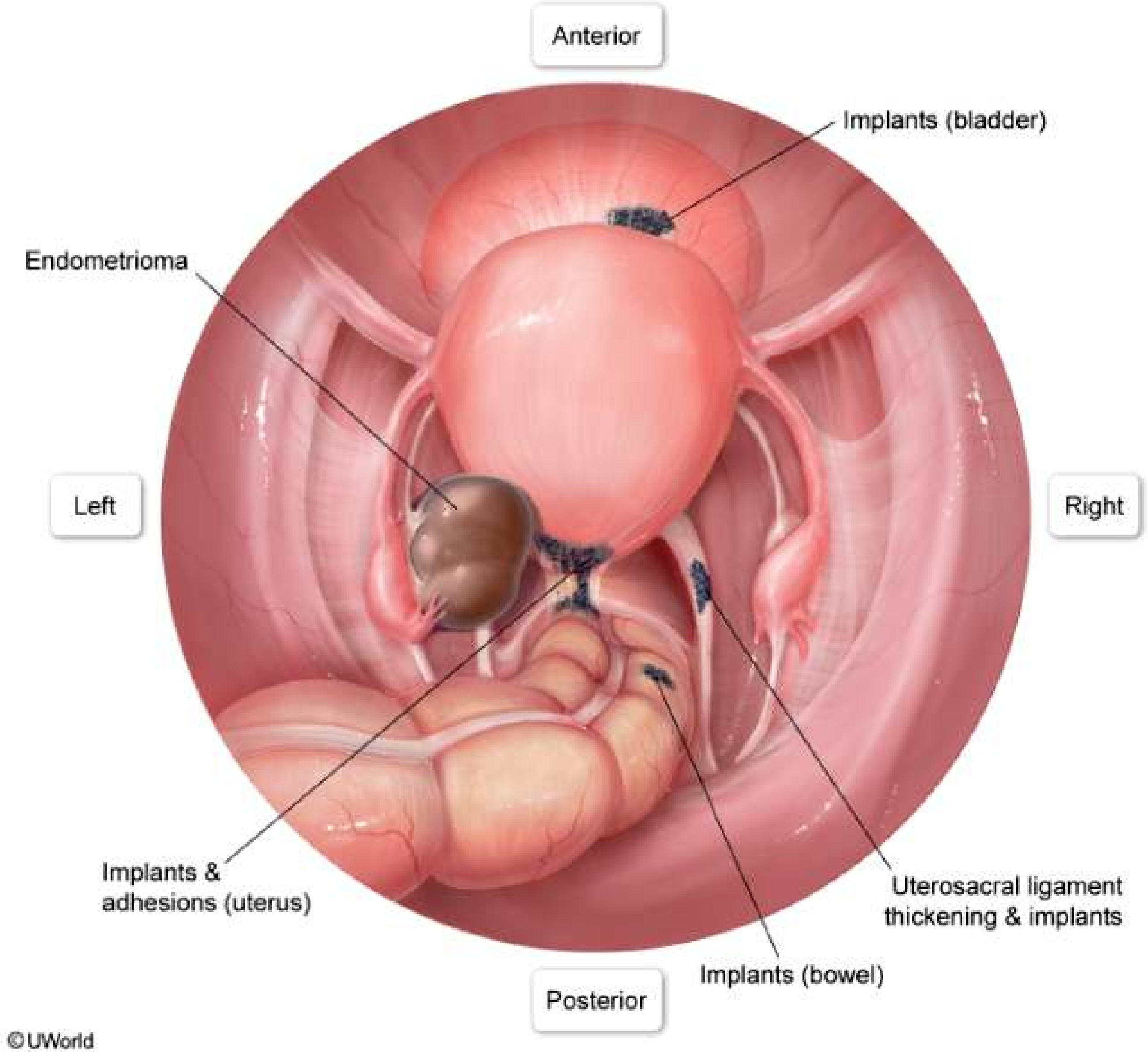
Explanation

Pelvic endometriosis

○ D. Invasive urothelial carcinoma (2%)

Exhibit Display

Pelvic endometriosis


Anterior
Implants (bladder)
Endometrioma
Left
Right
Implants & adhesions (uterus)
Uterosacral ligament thickening & implants
Implants (bowel)
Posterior

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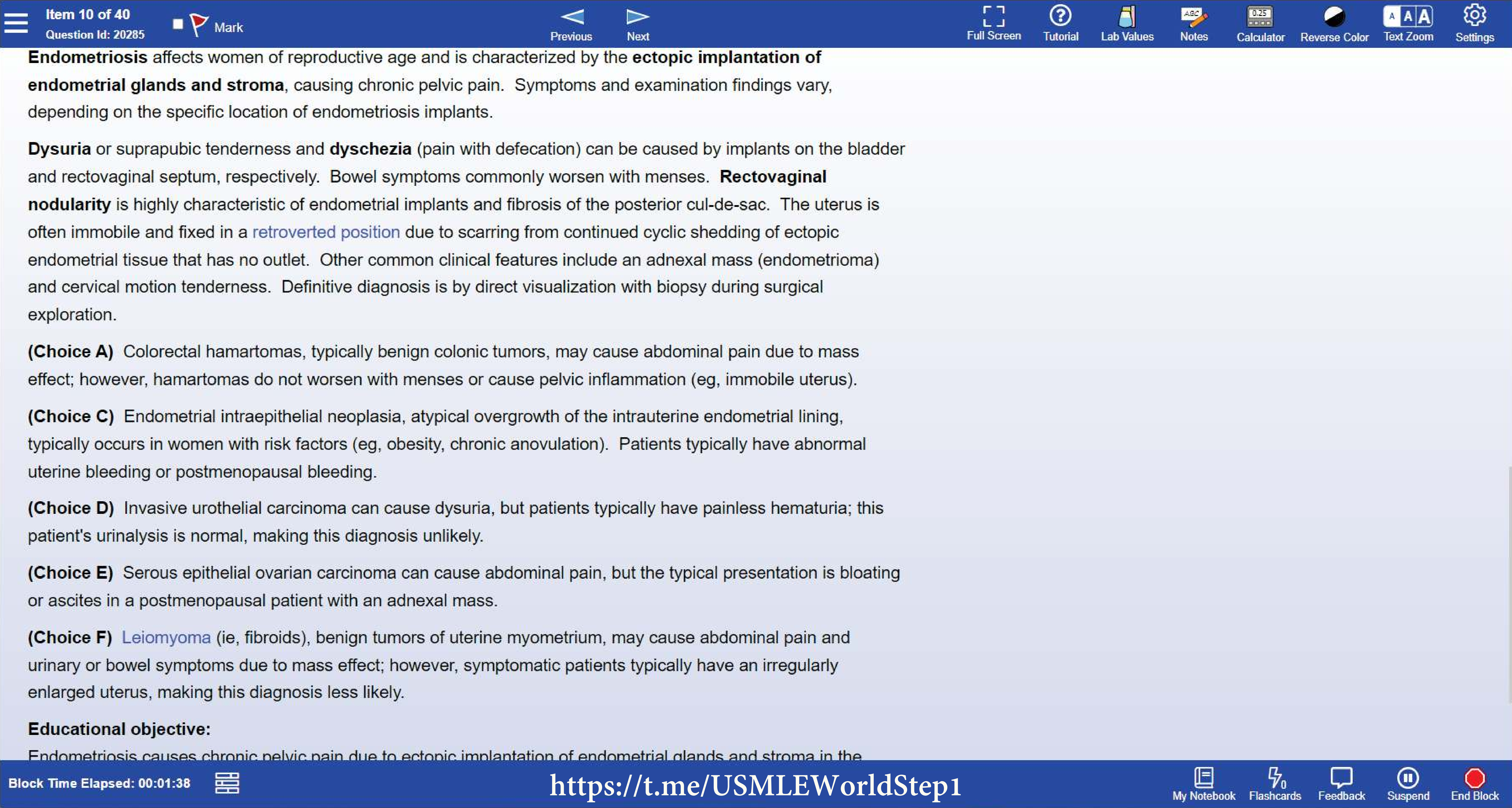

Endometriosis affects women of reproductive age and is characterized by the **ectopic implantation of endometrial glands and stroma**, causing chronic pelvic pain. Symptoms and examination findings vary, depending on the specific location of endometriosis implants.

Dysuria or suprapubic tenderness and **dyschezia** (pain with defecation) can be caused by implants on the bladder and rectovaginal septum, respectively. Bowel symptoms commonly worsen with menses. **Rectovaginal nodularity** is highly characteristic of endometrial implants and fibrosis of the posterior cul-de-sac. The uterus is often immobile and fixed in a retroverted position due to scarring from continued cyclic shedding of ectopic endometrial tissue that has no outlet. Other common clinical features include an adnexal mass (endometrioma) and cervical motion tenderness. Definitive diagnosis is by direct visualization with biopsy during surgical exploration.

(Choice A) Colorectal hamartomas, typically benign colonic tumors, may cause abdominal pain due to mass effect; however, hamartomas do not worsen with menses or cause pelvic inflammation (eg, immobile uterus).

(Choice C) Endometrial intraepithelial neoplasia, atypical overgrowth of the intrauterine endometrial lining, typically occurs in women with risk factors (eg, obesity, chronic anovulation). Patients typically have abnormal uterine bleeding or postmenopausal bleeding.

(Choice D) Invasive urothelial carcinoma can cause dysuria, but patients typically have painless hematuria; this patient's urinalysis is normal, making this diagnosis unlikely.

(Choice E) Serous epithelial ovarian carcinoma can cause abdominal pain, but the typical presentation is bloating or ascites in a postmenopausal patient with an adnexal mass.

(Choice F) Leiomyoma (ie, fibroids), benign tumors of uterine myometrium, may cause abdominal pain and urinary or bowel symptoms due to mass effect; however, symptomatic patients typically have an irregularly enlarged uterus, making this diagnosis less likely.

Educational objective:

Endometriosis causes chronic pelvic pain due to ectopic implantation of endometrial glands and stroma in the

Dysuria or suprapubic tenderness and **dyschezia** (pain with defecation) can be caused by implants on the bladder and rectovaginal septum, respectively. Bowel symptoms commonly worsen with menses. **Rectovaginal nodularity** is highly characteristic of endometrial implants and fibrosis of the posterior cul-de-sac. The uterus is often immobile and fixed in a retroverted position due to scarring from continued cyclic shedding of ectopic endometrial tissue that has no outlet. Other common clinical features include an adnexal mass (endometrioma) and cervical motion tenderness. Definitive diagnosis is by direct visualization with biopsy during surgical exploration.

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(Choice E) Serous epithelial ovarian carcinoma can cause abdominal pain, but the typical presentation is bloating or ascites in a postmenopausal patient with an adnexal mass.

(Choice F) Leiomyoma (ie, fibroids), benign tumors of uterine myometrium, may cause abdominal pain and urinary or bowel symptoms due to mass effect; however, symptomatic patients typically have an irregularly enlarged uterus, making this diagnosis less likely.

Educational objective:

Endometriosis causes chronic pelvic pain due to ectopic implantation of endometrial glands and stroma in the abdominopelvic cavity. Bladder implants may also result in dysuria while rectovaginal implants may cause dyschezia, rectovaginal nodularity, and pelvic fibrosis (eg, immobile uterus).

Implants (bowel)

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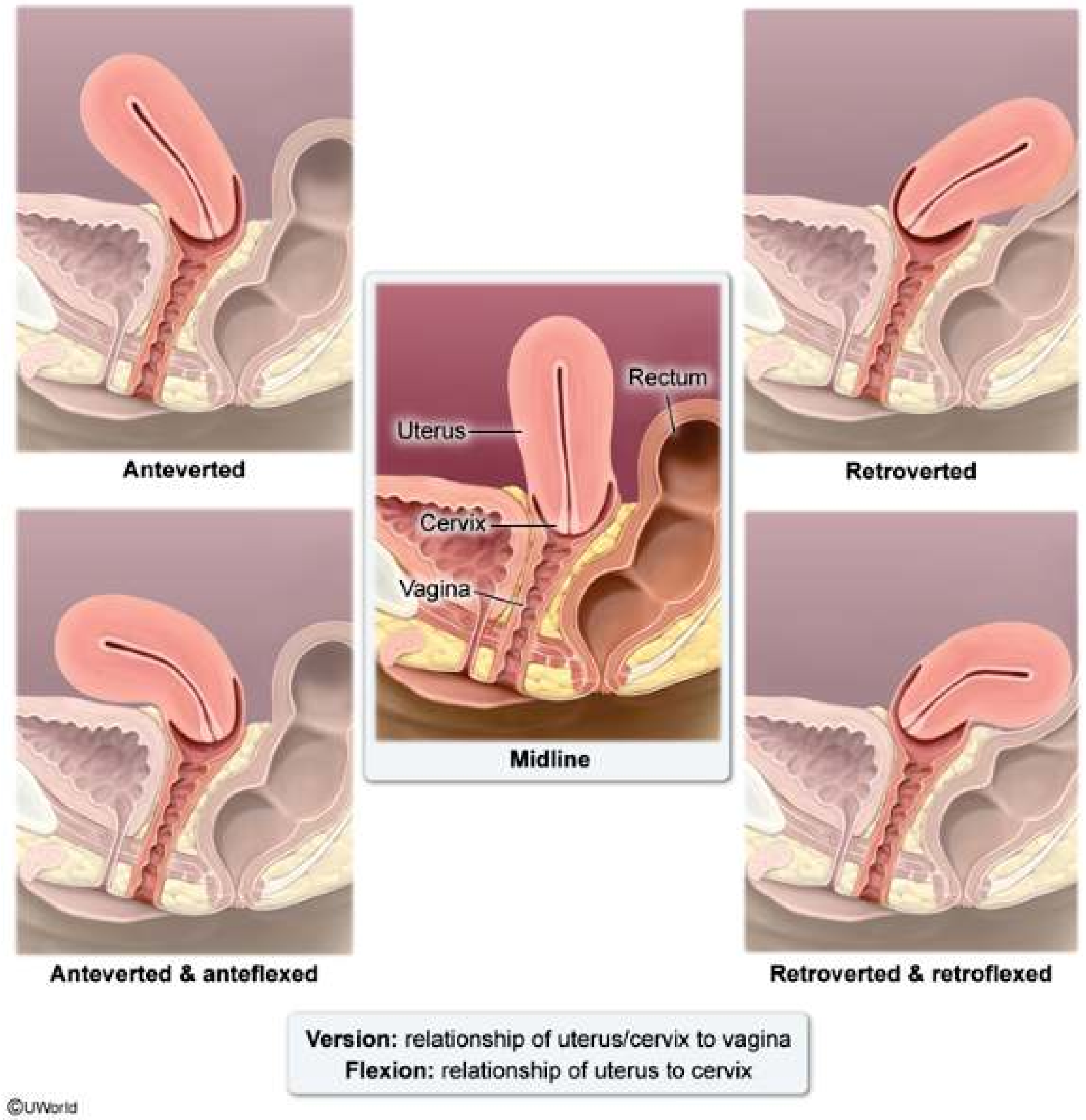
Uterine positioning


Anteverted
Retroverted
Rectum
Uterus
Cervix
Vagina
Midline
Anteverted & anteflexed
Retroverted & retroflexed
Version: relationship of uterus/cervix to vagina
Flexion: relationship of uterus to cervix
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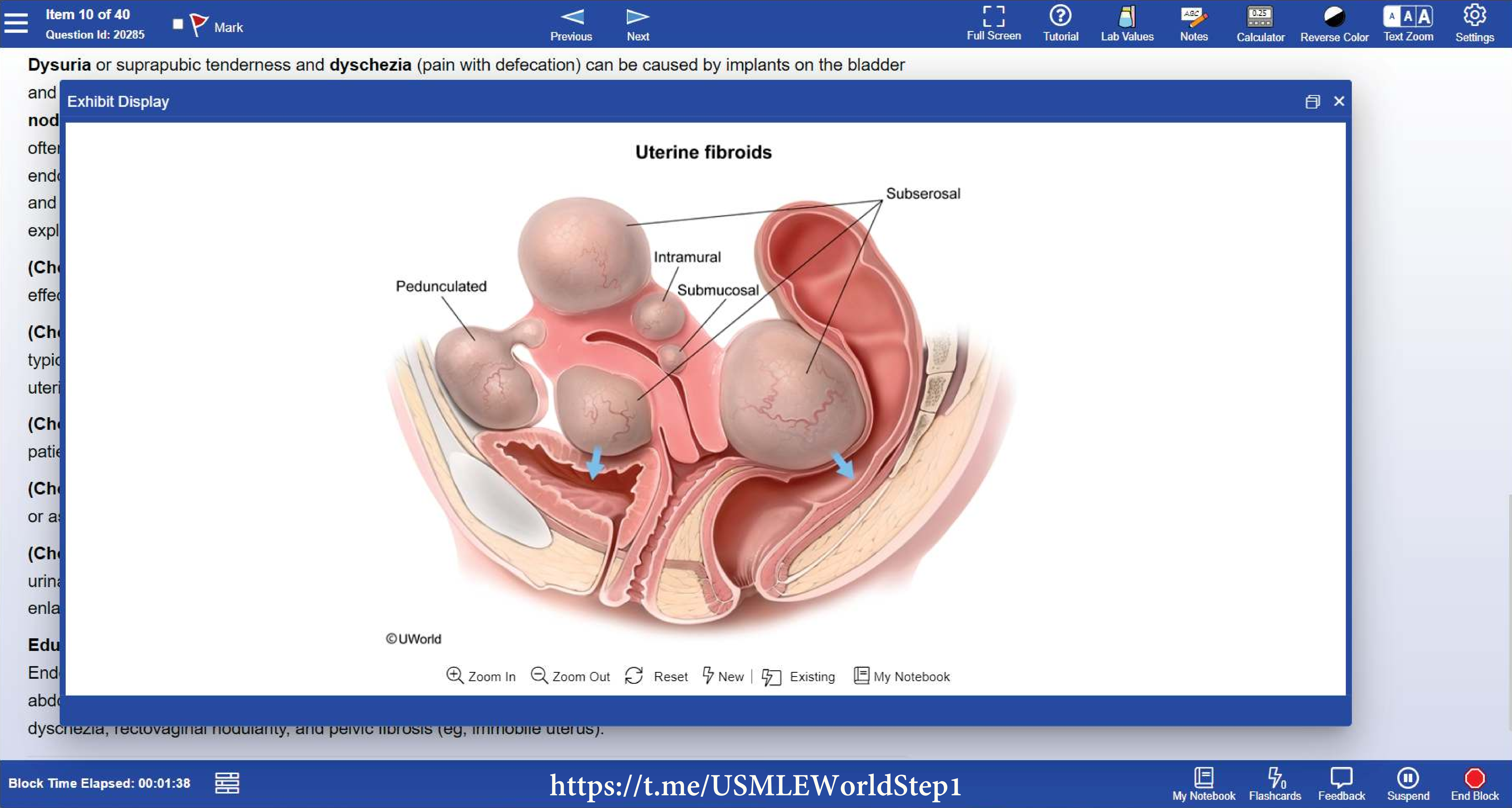
urinary or bowel symptoms due to mass effect; however, symptomatic patients typically have an irregularly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Dysuria or suprapubic tenderness and **dyschezia** (pain with defecation) can be caused by implants on the bladder

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dyschezia, rectovaginal nodularity, and pelvic fibrosis (eg, immobile uterus).

Uterine fibroids

Subserosal
Intramural
Submucosal
Pedunculated

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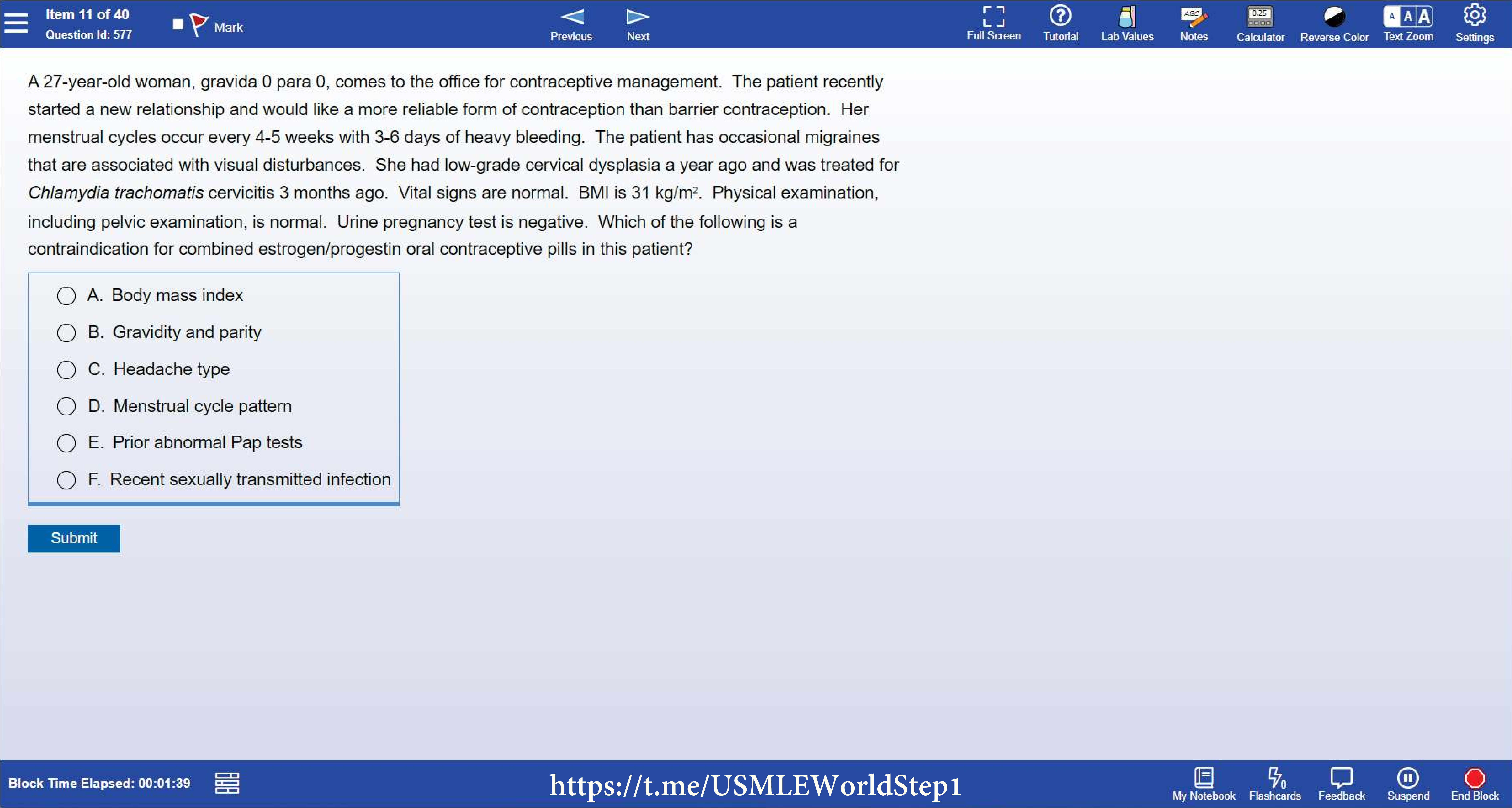
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A 27-year-old woman, gravida 0 para 0, comes to the office for contraceptive management. The patient recently started a new relationship and would like a more reliable form of contraception than barrier contraception. Her menstrual cycles occur every 4-5 weeks with 3-6 days of heavy bleeding. The patient has occasional migraines that are associated with visual disturbances. She had low-grade cervical dysplasia a year ago and was treated for *Chlamydia trachomatis* cervicitis 3 months ago. Vital signs are normal. BMI is 31 kg/m^2. Physical examination, including pelvic examination, is normal. Urine pregnancy test is negative. Which of the following is a contraindication for combined estrogen/progestin oral contraceptive pills in this patient?

○ A. Body mass index
○ B. Gravidity and parity
○ C. Headache type
○ D. Menstrual cycle pattern
○ E. Prior abnormal Pap tests
○ F. Recent sexually transmitted infection

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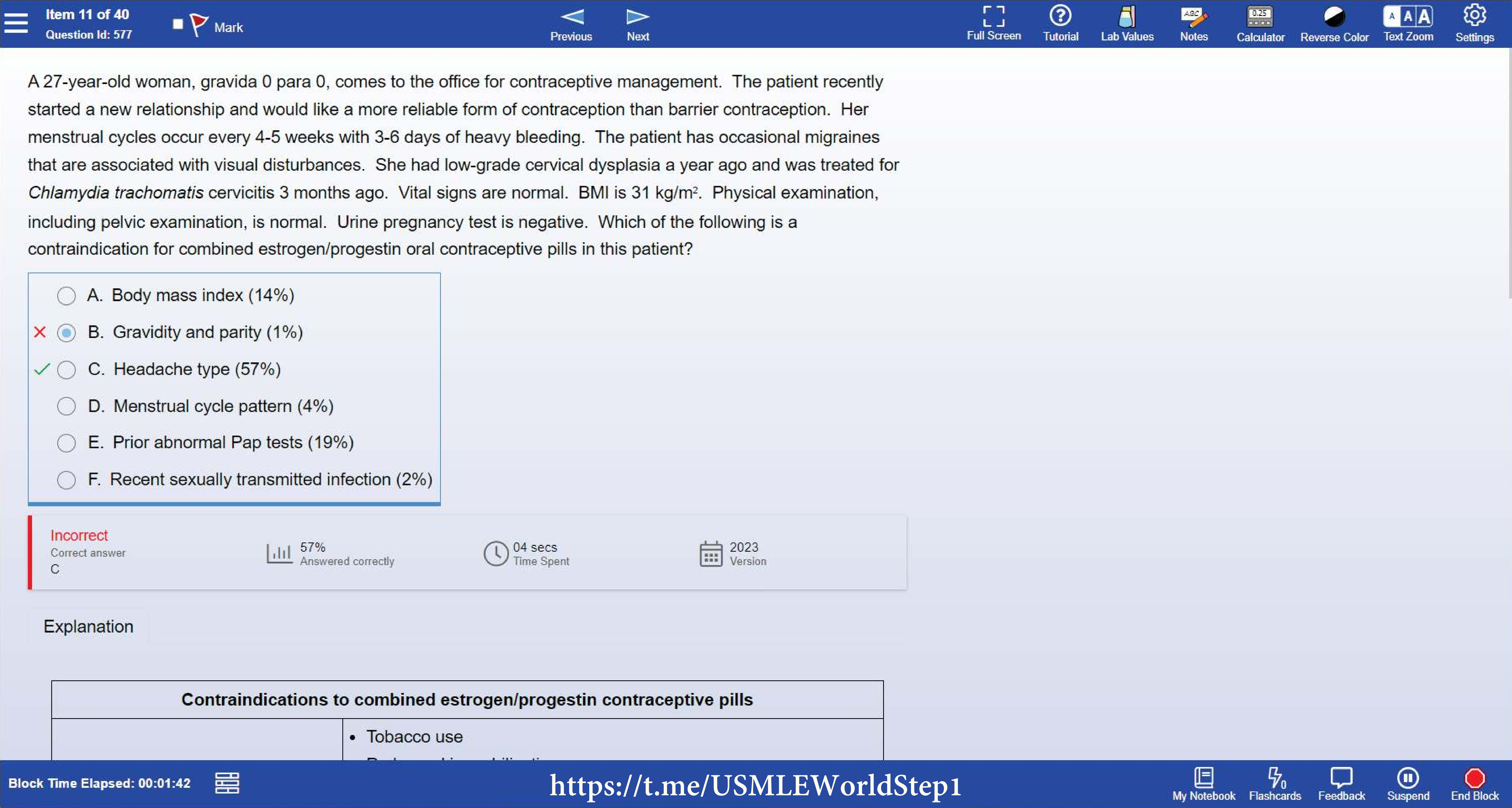
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- ○ A. Body mass index (14%)
- ✗ ● B. Gravidity and parity (1%)
- ✓ ○ C. Headache type (57%)
- ○ D. Menstrual cycle pattern (4%)
- ○ E. Prior abnormal Pap tests (19%)
- ○ F. Recent sexually transmitted infection (2%)

Incorrect
Correct answer
C

57%
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Explanation

Contraindications to combined estrogen/progestin contraceptive pills	
	• Tobacco use

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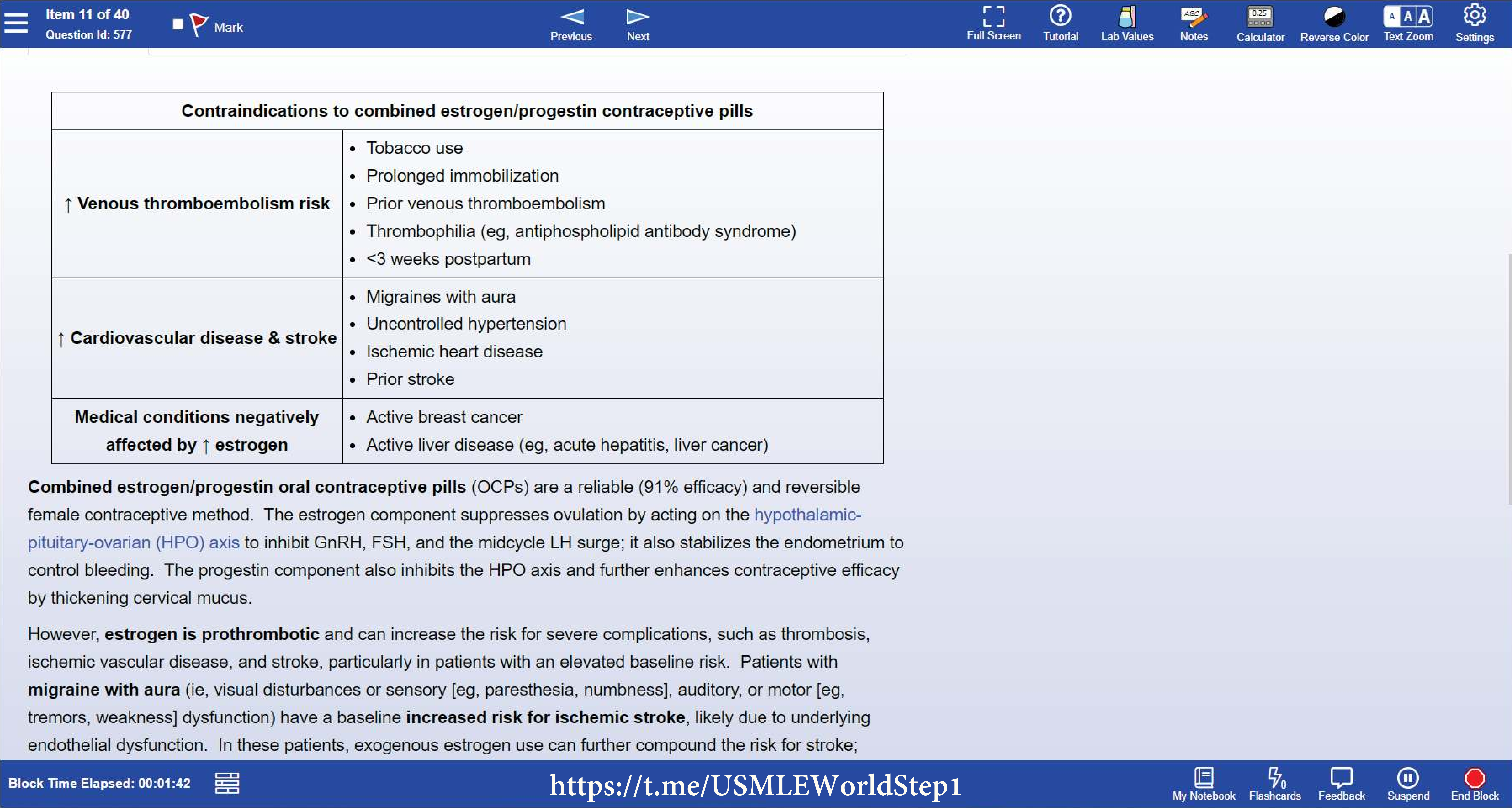
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Contraindications to combined estrogen/progestin contraceptive pills	
↑ Venous thromboembolism risk	Tobacco use Prolonged immobilization Prior venous thromboembolism Thrombophilia (eg, antiphospholipid antibody syndrome) <3 weeks postpartum
↑ Cardiovascular disease & stroke	Migraines with aura Uncontrolled hypertension Ischemic heart disease Prior stroke
Medical conditions negatively affected by ↑ estrogen	Active breast cancer Active liver disease (eg, acute hepatitis, liver cancer)

Combined estrogen/progestin oral contraceptive pills (OCPs) are a reliable (91% efficacy) and reversible female contraceptive method. The estrogen component suppresses ovulation by acting on the hypothalamic-pituitary-ovarian (HPO) axis to inhibit GnRH, FSH, and the midcycle LH surge; it also stabilizes the endometrium to control bleeding. The progestin component also inhibits the HPO axis and further enhances contraceptive efficacy by thickening cervical mucus.

However, **estrogen is prothrombotic** and can increase the risk for severe complications, such as thrombosis, ischemic vascular disease, and stroke, particularly in patients with an elevated baseline risk. Patients with **migraine with aura** (ie, visual disturbances or sensory [eg, paresthesia, numbness], auditory, or motor [eg, tremors, weakness] dysfunction) have a baseline **increased risk for ischemic stroke**, likely due to underlying endothelial dysfunction. In these patients, exogenous estrogen use can further compound the risk for stroke;

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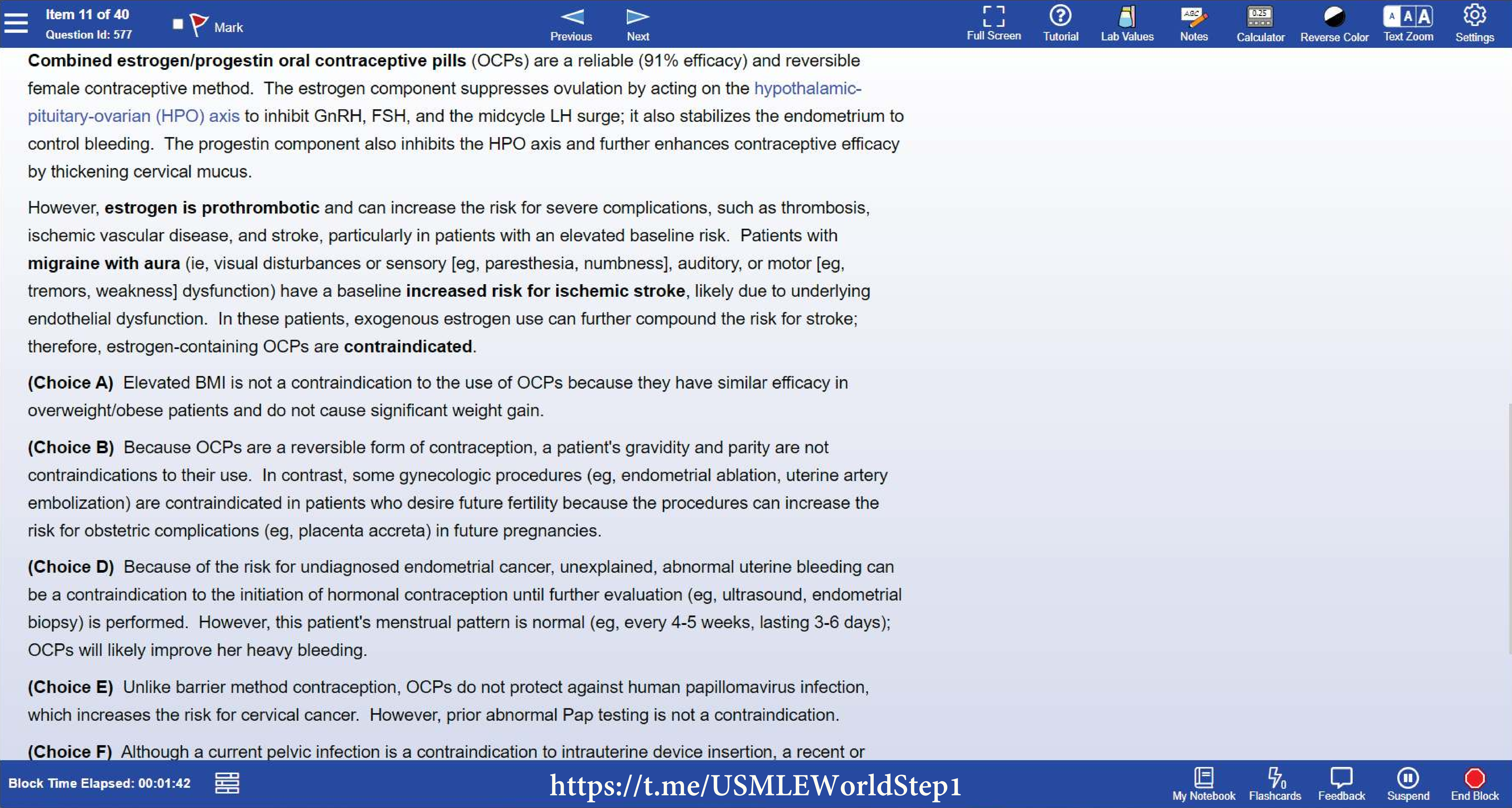

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(Choice A) Elevated BMI is not a contraindication to the use of OCPs because they have similar efficacy in overweight/obese patients and do not cause significant weight gain.

(Choice B) Because OCPs are a reversible form of contraception, a patient's gravidity and parity are not contraindications to their use. In contrast, some gynecologic procedures (eg, endometrial ablation, uterine artery embolization) are contraindicated in patients who desire future fertility because the procedures can increase the risk for obstetric complications (eg, placenta accreta) in future pregnancies.

(Choice D) Because of the risk for undiagnosed endometrial cancer, unexplained, abnormal uterine bleeding can be a contraindication to the initiation of hormonal contraception until further evaluation (eg, ultrasound, endometrial biopsy) is performed. However, this patient's menstrual pattern is normal (eg, every 4-5 weeks, lasting 3-6 days); OCPs will likely improve her heavy bleeding.

(Choice E) Unlike barrier method contraception, OCPs do not protect against human papillomavirus infection, which increases the risk for cervical cancer. However, prior abnormal Pap testing is not a contraindication.

(Choice F) Although a current pelvic infection is a contraindication to intrauterine device insertion, a recent or

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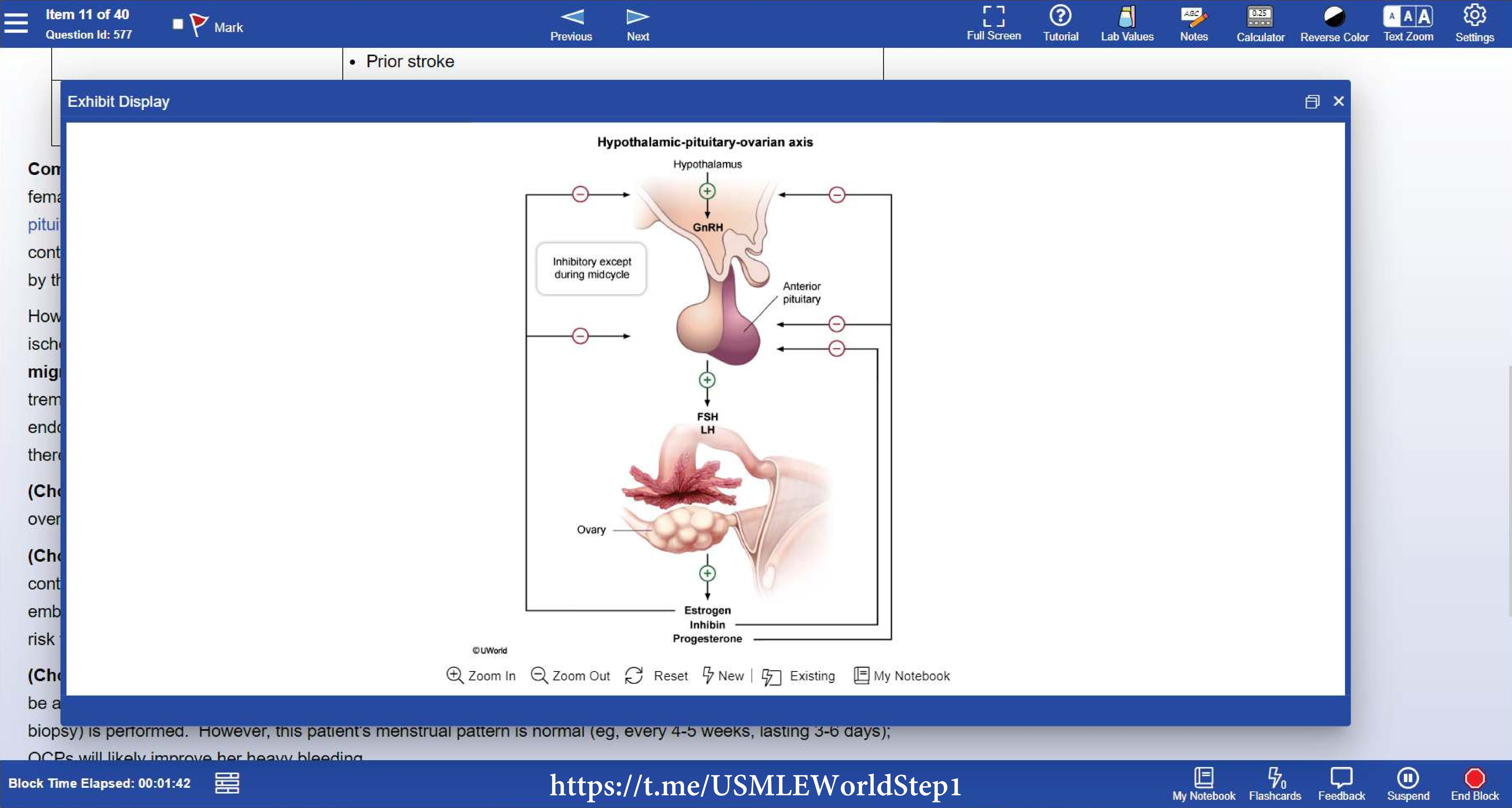
(Choice E) Unlike barrier method contraception, OCPs do not protect against human papillomavirus infection, which increases the risk for cervical cancer. However, prior abnormal Pap testing is not a contraindication.

(Choice F) Although a current pelvic infection is a contraindication to intrauterine device insertion, a recent or current sexually transmitted infection is not a contraindication to initiating OCPs.

Educational objective:

Estrogen-containing contraceptive pills (eg, combined estrogen/progestin oral contraceptive pills) are contraindicated in patients with migraine with aura due to the increased risk for ischemic stroke.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Hypothalamic-pituitary-ovarian axis
Hypothalamus
GnRH
Inhibitory except during midcycle
Anterior pituitary
FSH
LH
Ovary
Estrogen
Inhibin
Progesterone
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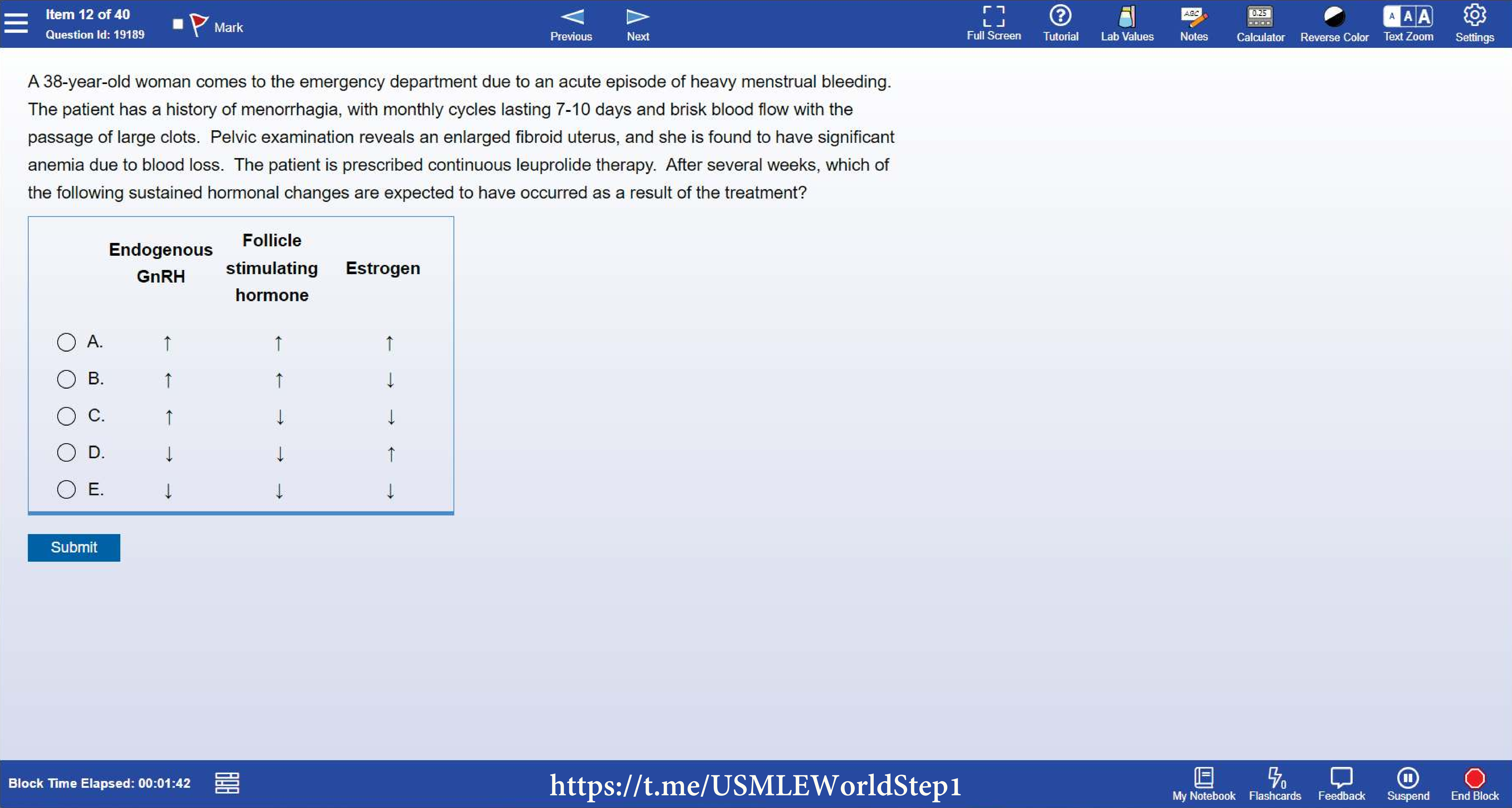
biopsy) is performed. However, this patient's menstrual pattern is normal (eg, every 4-5 weeks, lasting 3-6 days);
OCPs will likely improve her heavy bleeding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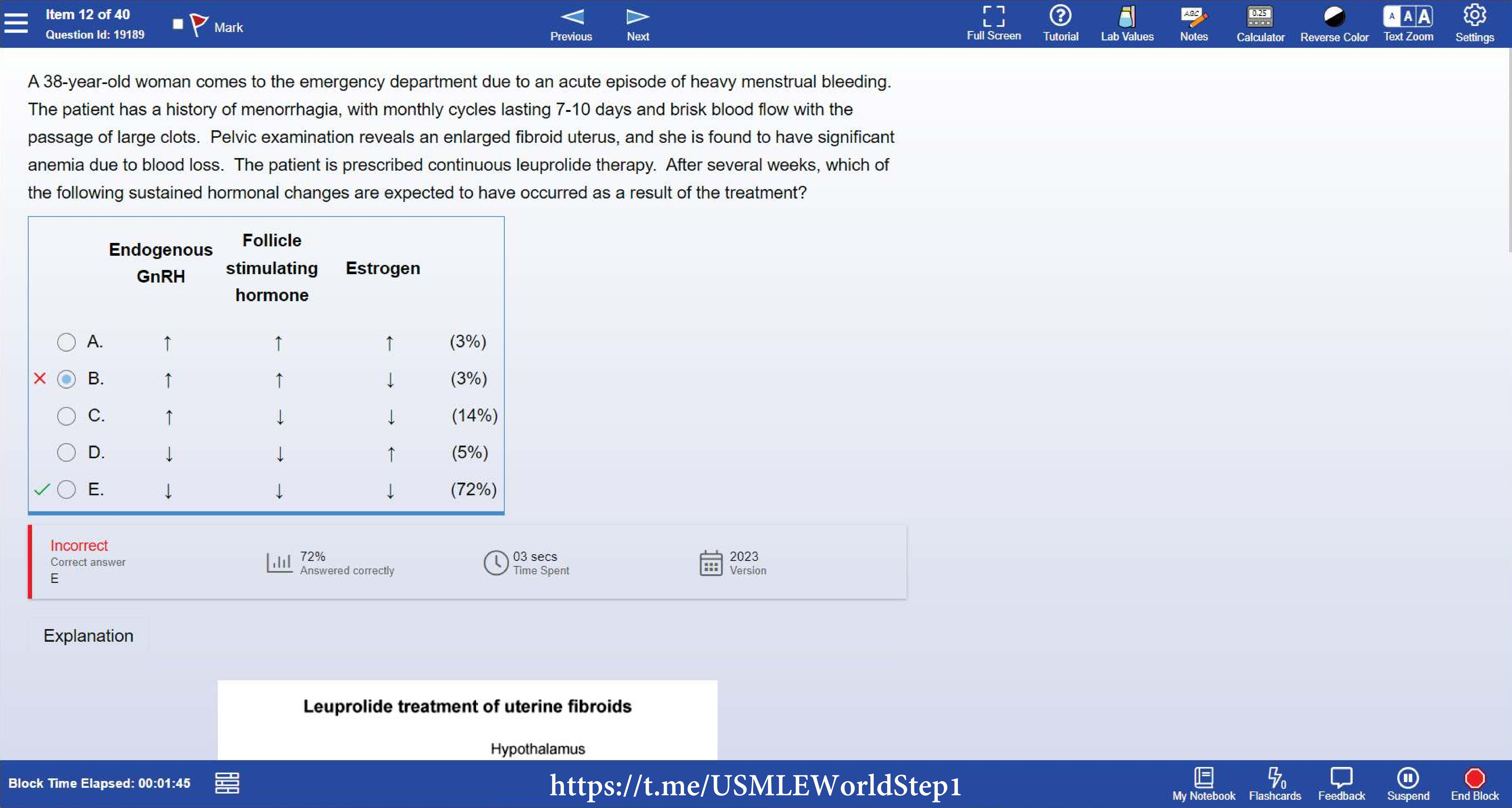
A 38-year-old woman comes to the emergency department due to an acute episode of heavy menstrual bleeding. The patient has a history of menorrhagia, with monthly cycles lasting 7-10 days and brisk blood flow with the passage of large clots. Pelvic examination reveals an enlarged fibroid uterus, and she is found to have significant anemia due to blood loss. The patient is prescribed continuous leuprolide therapy. After several weeks, which of the following sustained hormonal changes are expected to have occurred as a result of the treatment?

	Endogenous GnRH	Follicle stimulating hormone	Estrogen
○ A.	↑	↑	↑
○ B.	↑	↑	↓
○ C.	↑	↓	↓
○ D.	↓	↓	↑
○ E.	↓	↓	↓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A 38-year-old woman comes to the emergency department due to an acute episode of heavy menstrual bleeding. The patient has a history of menorrhagia, with monthly cycles lasting 7-10 days and brisk blood flow with the passage of large clots. Pelvic examination reveals an enlarged fibroid uterus, and she is found to have significant anemia due to blood loss. The patient is prescribed continuous leuprolide therapy. After several weeks, which of the following sustained hormonal changes are expected to have occurred as a result of the treatment?

		Endogenous GnRH	Follicle stimulating hormone	Estrogen	
	○ A.	↑	↑	↑	(3%)
×	● B.	↑	↑	↓	(3%)
	○ C.	↑	↓	↓	(14%)
	○ D.	↓	↓	↑	(5%)
✓	○ E.	↓	↓	↓	(72%)

Incorrect
Correct answer
E

72%
Answered correctly

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Explanation

Leuprolide treatment of uterine fibroids

Hypothalamus

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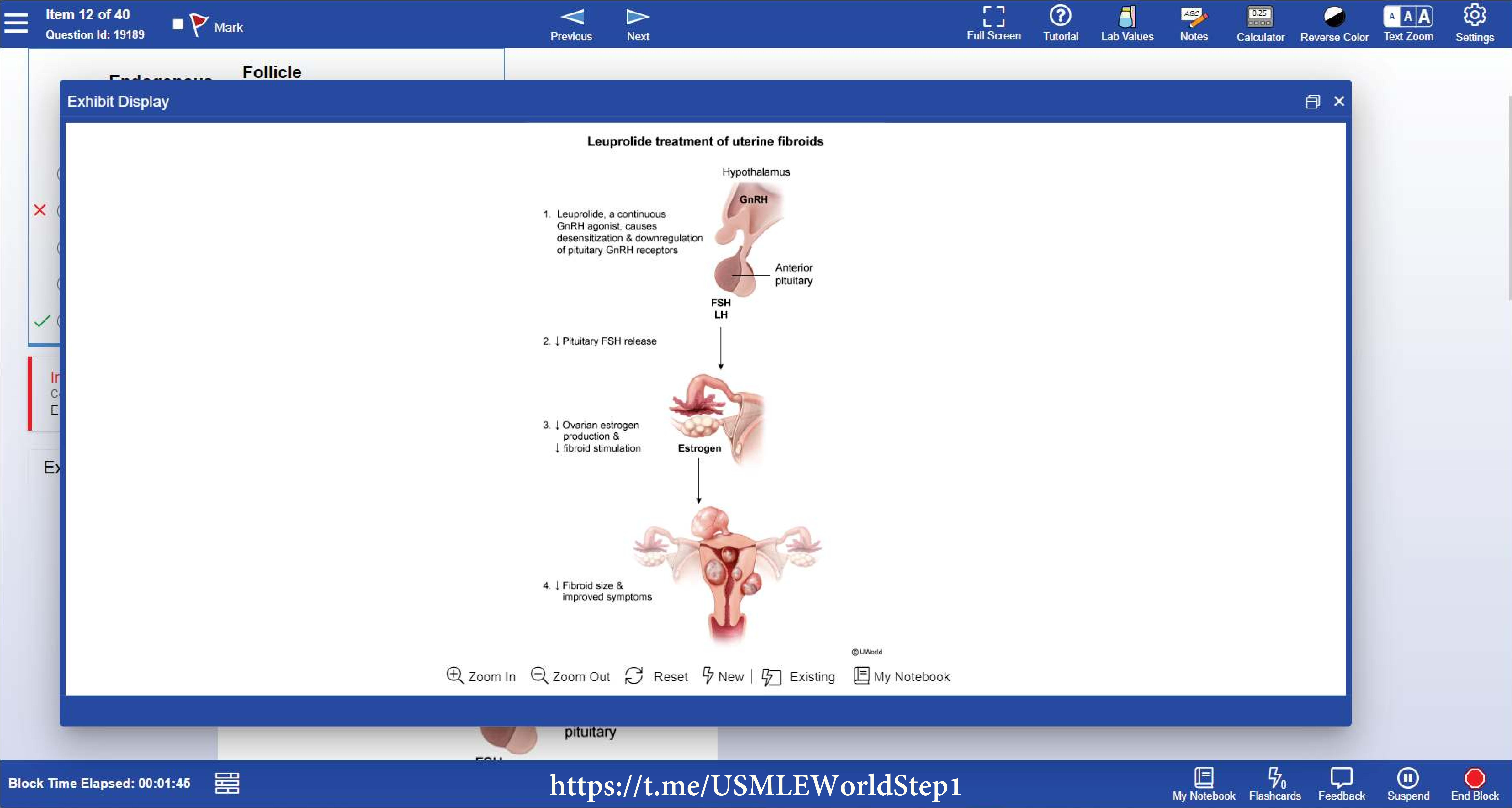
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pituitary
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Leuprolide treatment of uterine fibroids

Hypothalamus
GnRH
Anterior pituitary
FSH
LH
Estrogen
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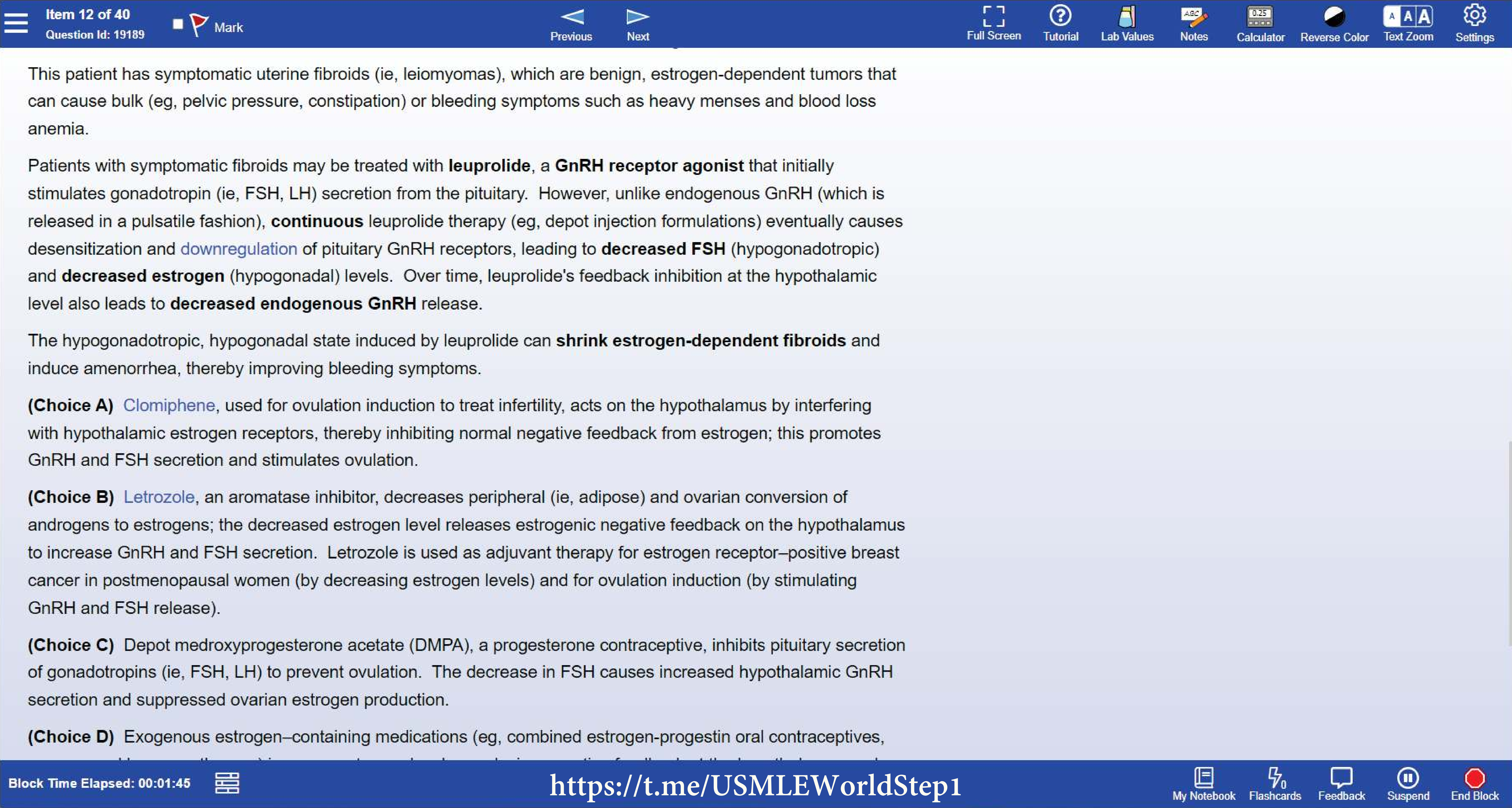
1. Leuprolide, a continuous GnRH agonist, causes desensitization & downregulation of pituitary GnRH receptors
2. ↓ Pituitary FSH release
3. ↓ Ovarian estrogen production & ↓ fibroid stimulation
4. ↓ Fibroid size & improved symptoms



This patient has symptomatic uterine fibroids (ie, leiomyomas), which are benign, estrogen-dependent tumors that can cause bulk (eg, pelvic pressure, constipation) or bleeding symptoms such as heavy menses and blood loss anemia.

Patients with symptomatic fibroids may be treated with **leuprolide**, a **GnRH receptor agonist** that initially stimulates gonadotropin (ie, FSH, LH) secretion from the pituitary. However, unlike endogenous GnRH (which is released in a pulsatile fashion), **continuous** leuprolide therapy (eg, depot injection formulations) eventually causes desensitization and downregulation of pituitary GnRH receptors, leading to **decreased FSH** (hypogonadotropic) and **decreased estrogen** (hypogonadal) levels. Over time, leuprolide's feedback inhibition at the hypothalamic level also leads to **decreased endogenous GnRH** release.

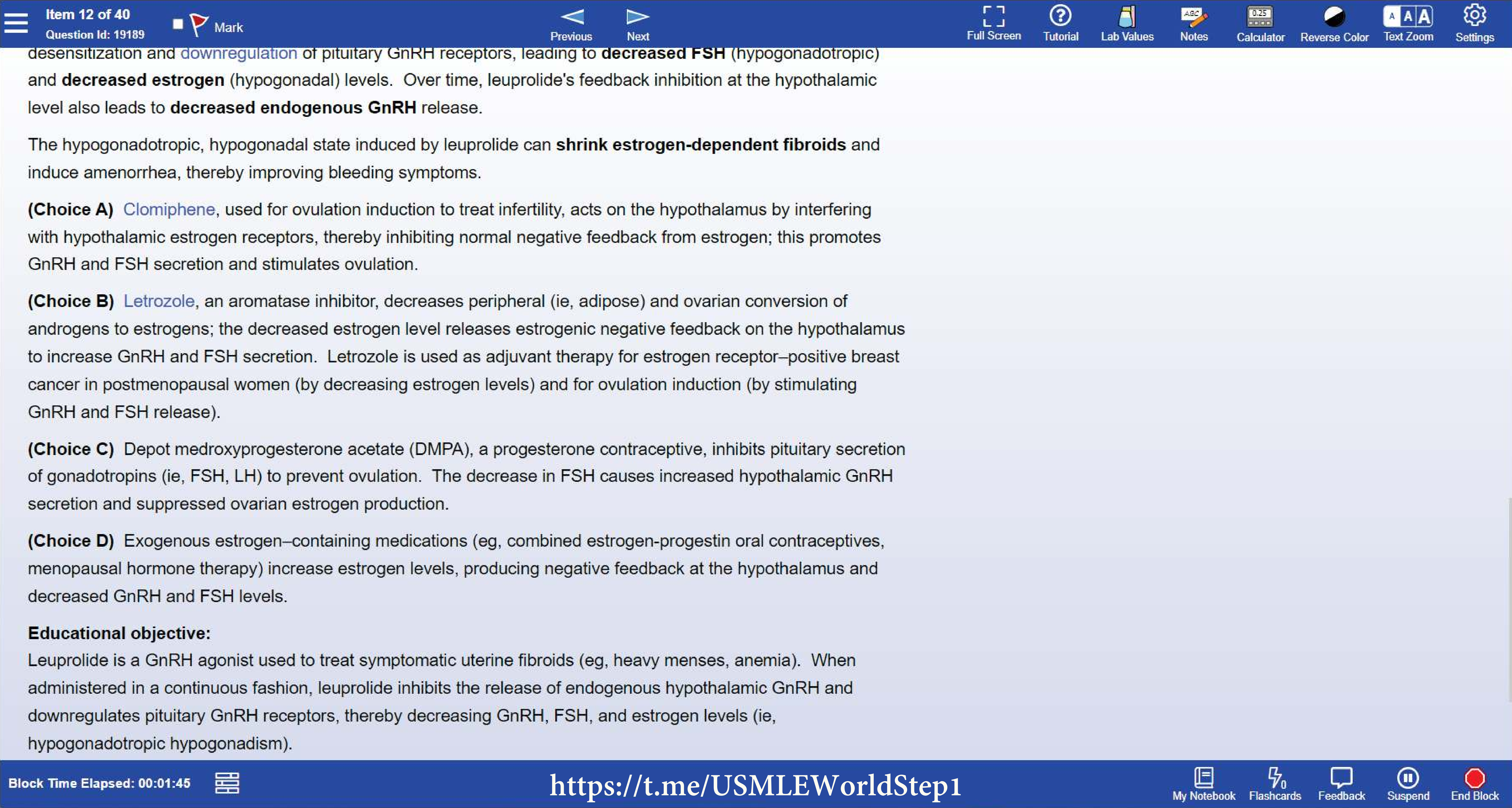
The hypogonadotropic, hypogonadal state induced by leuprolide can **shrink estrogen-dependent fibroids** and induce amenorrhea, thereby improving bleeding symptoms.

(Choice A) Clomiphene, used for ovulation induction to treat infertility, acts on the hypothalamus by interfering with hypothalamic estrogen receptors, thereby inhibiting normal negative feedback from estrogen; this promotes GnRH and FSH secretion and stimulates ovulation.

(Choice B) Letrozole, an aromatase inhibitor, decreases peripheral (ie, adipose) and ovarian conversion of androgens to estrogens; the decreased estrogen level releases estrogenic negative feedback on the hypothalamus to increase GnRH and FSH secretion. Letrozole is used as adjuvant therapy for estrogen receptor–positive breast cancer in postmenopausal women (by decreasing estrogen levels) and for ovulation induction (by stimulating GnRH and FSH release).

(Choice C) Depot medroxyprogesterone acetate (DMPA), a progesterone contraceptive, inhibits pituitary secretion of gonadotropins (ie, FSH, LH) to prevent ovulation. The decrease in FSH causes increased hypothalamic GnRH secretion and suppressed ovarian estrogen production.

(Choice D) Exogenous estrogen–containing medications (eg, combined estrogen-progestin oral contraceptives,



desensitization and downregulation of pituitary GnRH receptors, leading to **decreased FSH** (hypogonadotropic) and **decreased estrogen** (hypogonadal) levels. Over time, leuprolide's feedback inhibition at the hypothalamic level also leads to **decreased endogenous GnRH** release.

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(Choice D) Exogenous estrogen–containing medications (eg, combined estrogen-progestin oral contraceptives, menopausal hormone therapy) increase estrogen levels, producing negative feedback at the hypothalamus and decreased GnRH and FSH levels.

Educational objective:
Leuprolide is a GnRH agonist used to treat symptomatic uterine fibroids (eg, heavy menses, anemia). When administered in a continuous fashion, leuprolide inhibits the release of endogenous hypothalamic GnRH and downregulates pituitary GnRH receptors, thereby decreasing GnRH, FSH, and estrogen levels (ie, hypogonadotropic hypogonadism).

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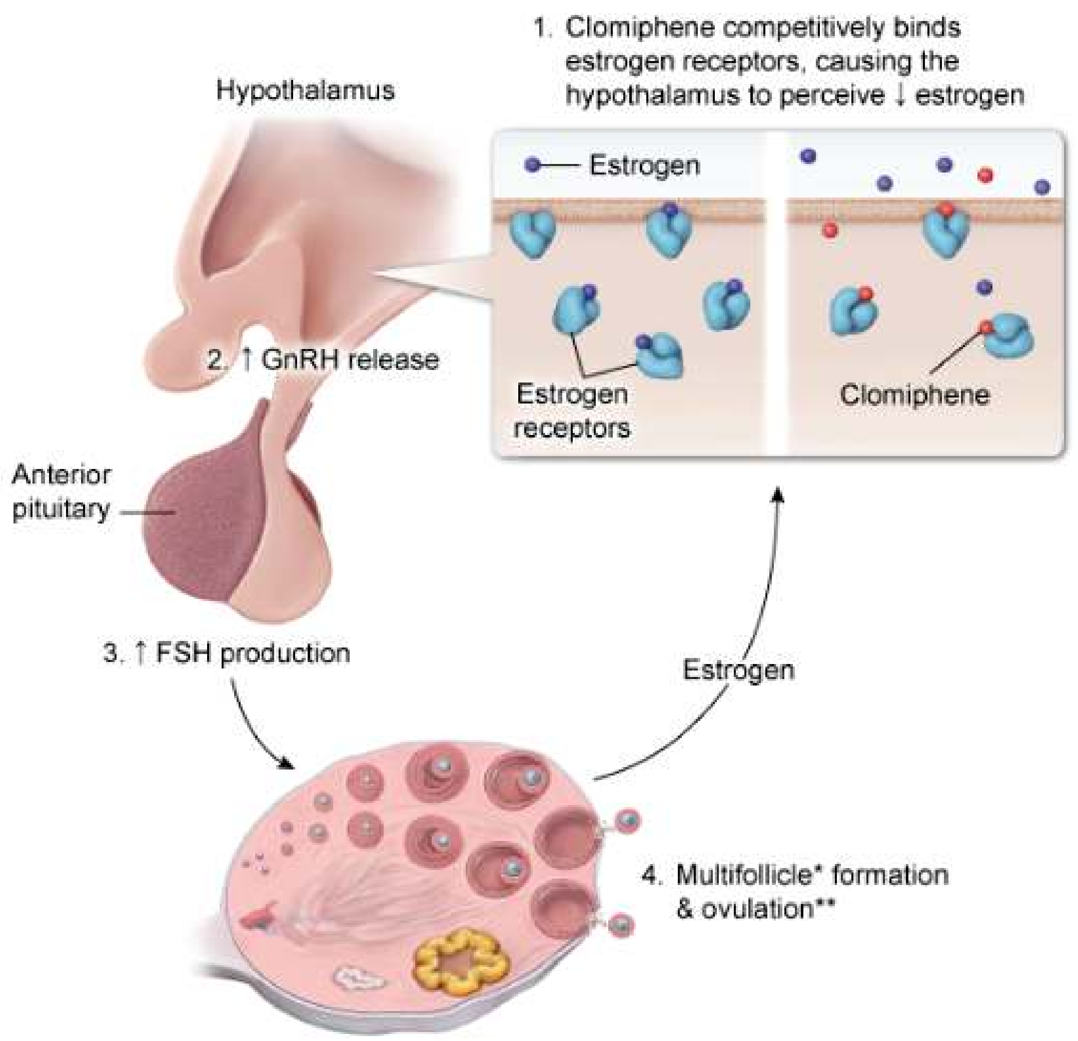
Clomiphene treatment of infertility


1. Clomiphene competitively binds estrogen receptors, causing the hypothalamus to perceive ↓ estrogen
Hypothalamus
Estrogen
Estrogen receptors
Clomiphene
2. ↑ GnRH release
Anterior pituitary
3. ↑ FSH production
Estrogen
4. Multifollicle* formation & ovulation**

*Follicular maturation ↑ estrogen, but clomiphene remains bound to estrogen receptors & causes continued GnRH & FSH release.
**Possible multifollicular development & release.

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(Choice C) Depot medroxyprogesterone acetate (DMPA), a progesterone contraceptive, inhibits pituitary secretion

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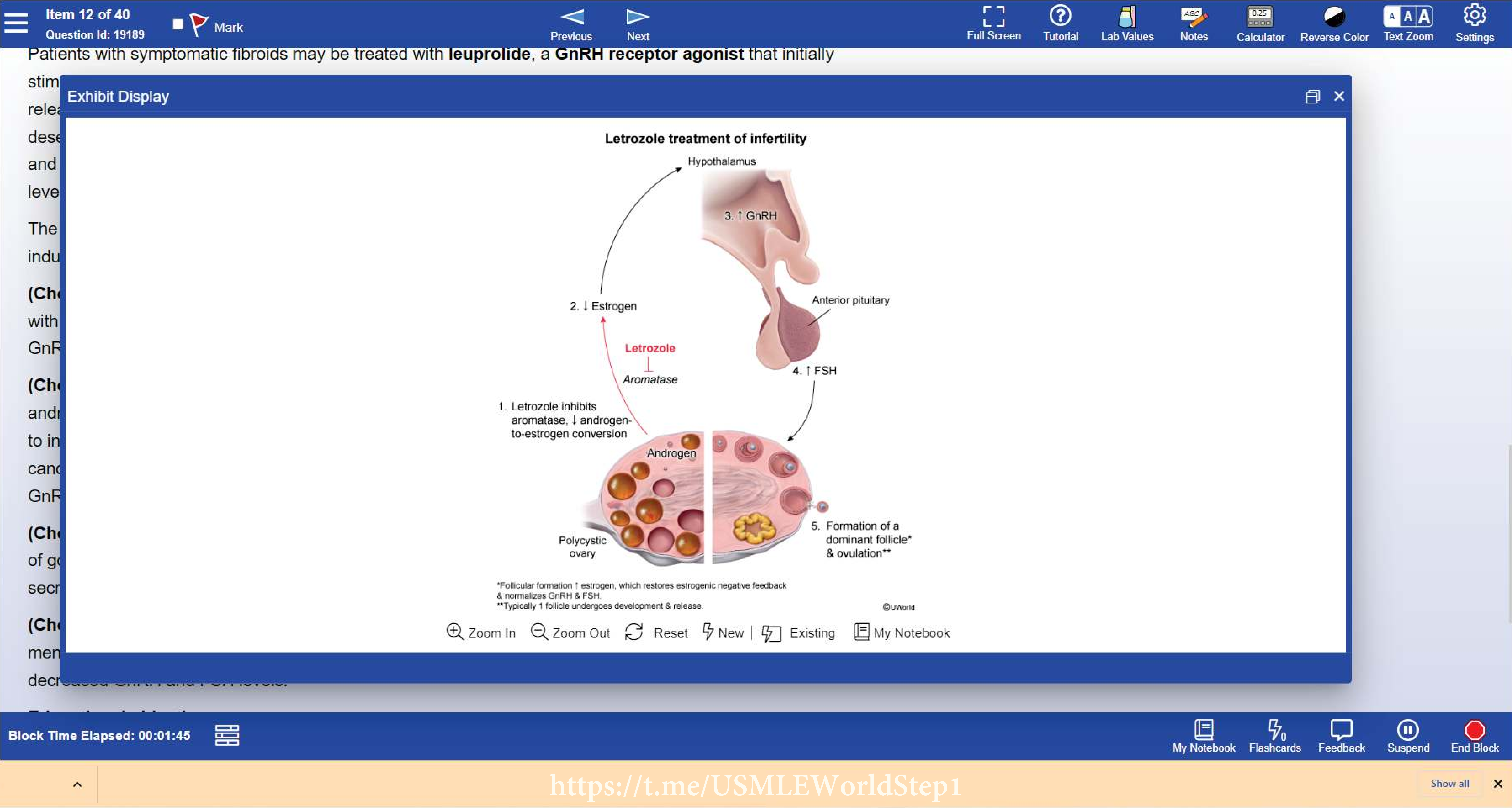

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Patients with symptomatic fibroids may be treated with **leuprolide**, a **GnRH receptor agonist** that initially

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Letrozole treatment of infertility

Hypothalamus
3. ↑ GnRH
Anterior pituitary
4. ↑ FSH
2. ↓ Estrogen
Letrozole
Aromatase
1. Letrozole inhibits aromatase, ↓ androgen-to-estrogen conversion
Androgen
Polycystic ovary
5. Formation of a dominant follicle* & ovulation**

*Follicular formation ↑ estrogen, which restores estrogenic negative feedback & normalizes GnRH & FSH.
**Typically 1 follicle undergoes development & release.

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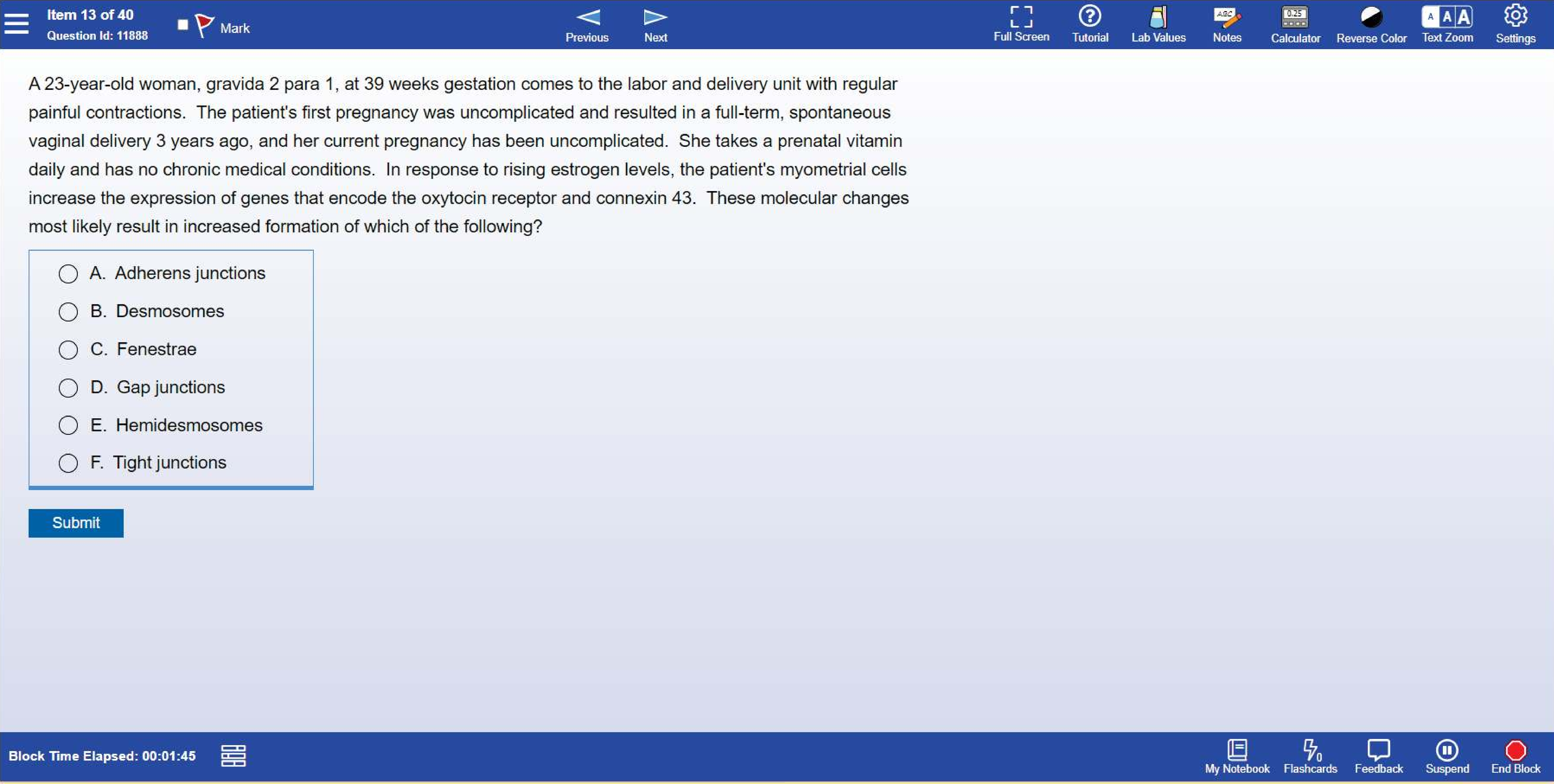
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A 23-year-old woman, gravida 2 para 1, at 39 weeks gestation comes to the labor and delivery unit with regular painful contractions. The patient's first pregnancy was uncomplicated and resulted in a full-term, spontaneous vaginal delivery 3 years ago, and her current pregnancy has been uncomplicated. She takes a prenatal vitamin daily and has no chronic medical conditions. In response to rising estrogen levels, the patient's myometrial cells increase the expression of genes that encode the oxytocin receptor and connexin 43. These molecular changes most likely result in increased formation of which of the following?

- ○ A. Adherens junctions
- ○ B. Desmosomes
- ○ C. Fenestrae
- ○ D. Gap junctions
- ○ E. Hemidesmosomes
- ○ F. Tight junctions

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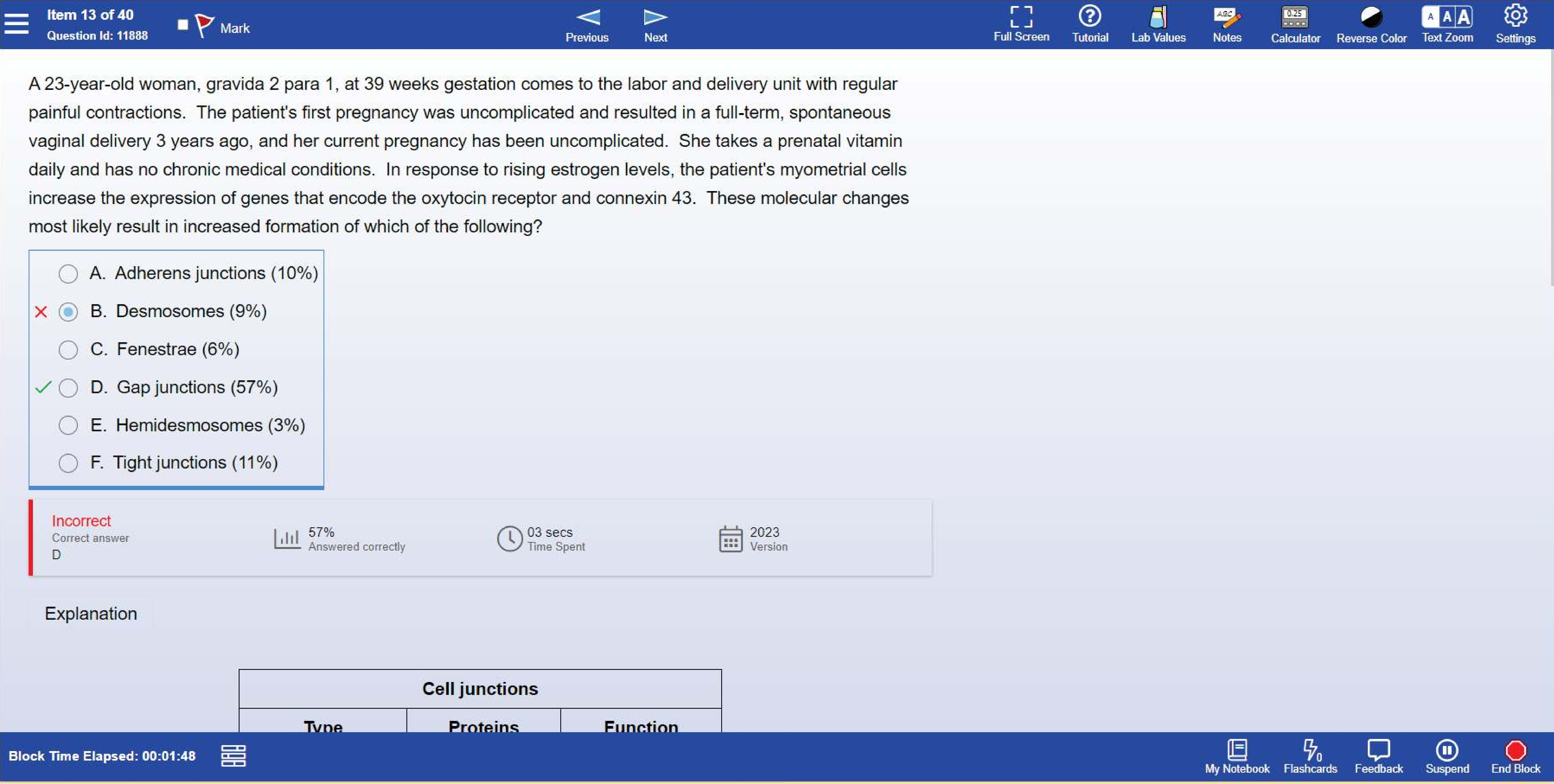
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- ○ A. Adherens junctions (10%)
- ✗ ● B. Desmosomes (9%)
- ○ C. Fenestrae (6%)
- ✓ ○ D. Gap junctions (57%)
- ○ E. Hemidesmosomes (3%)
- ○ F. Tight junctions (11%)

Incorrect
Correct answer
D

57%
Answered correctly

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Explanation

Cell junctions		
Type	Proteins	Function

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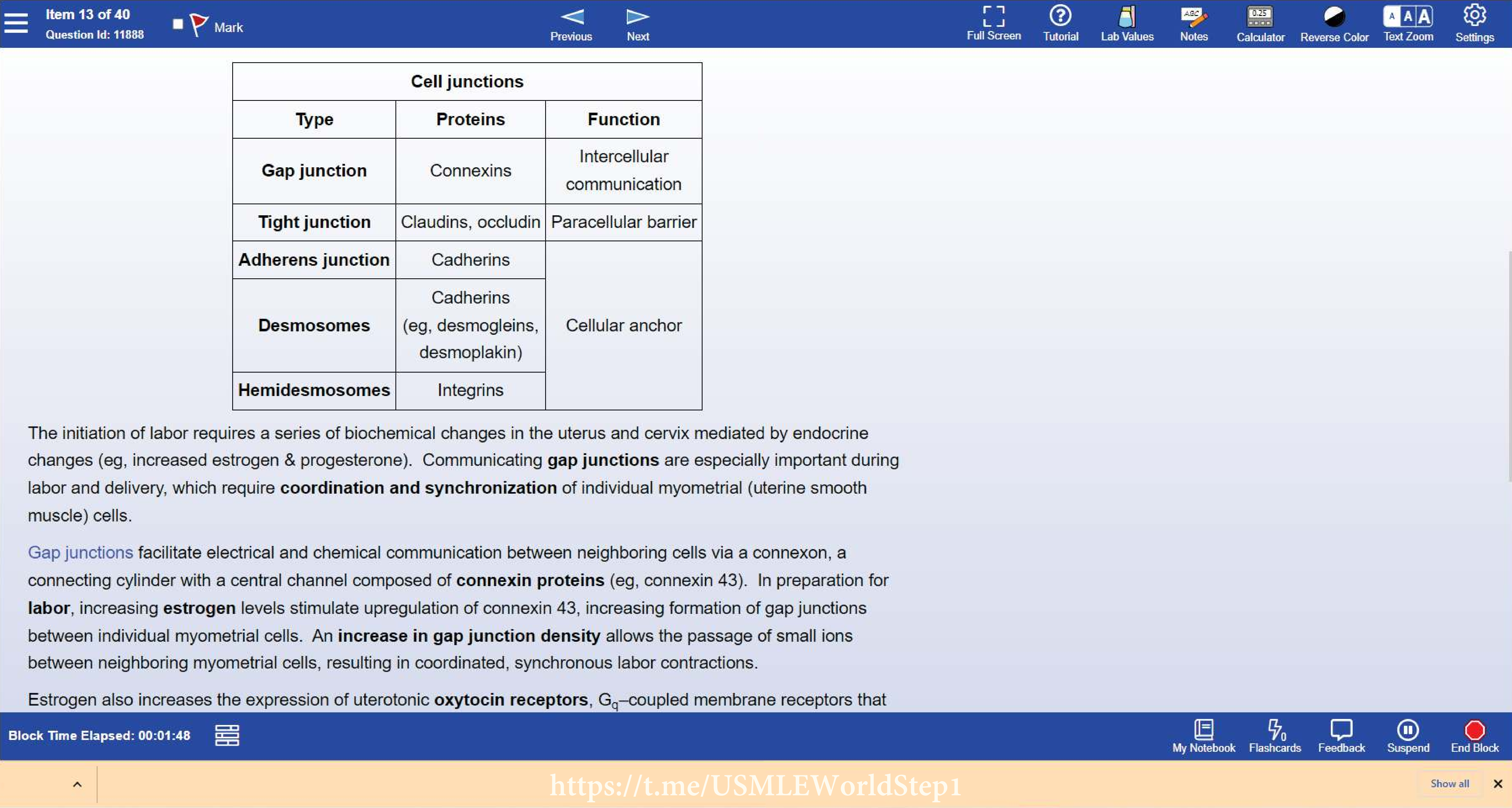
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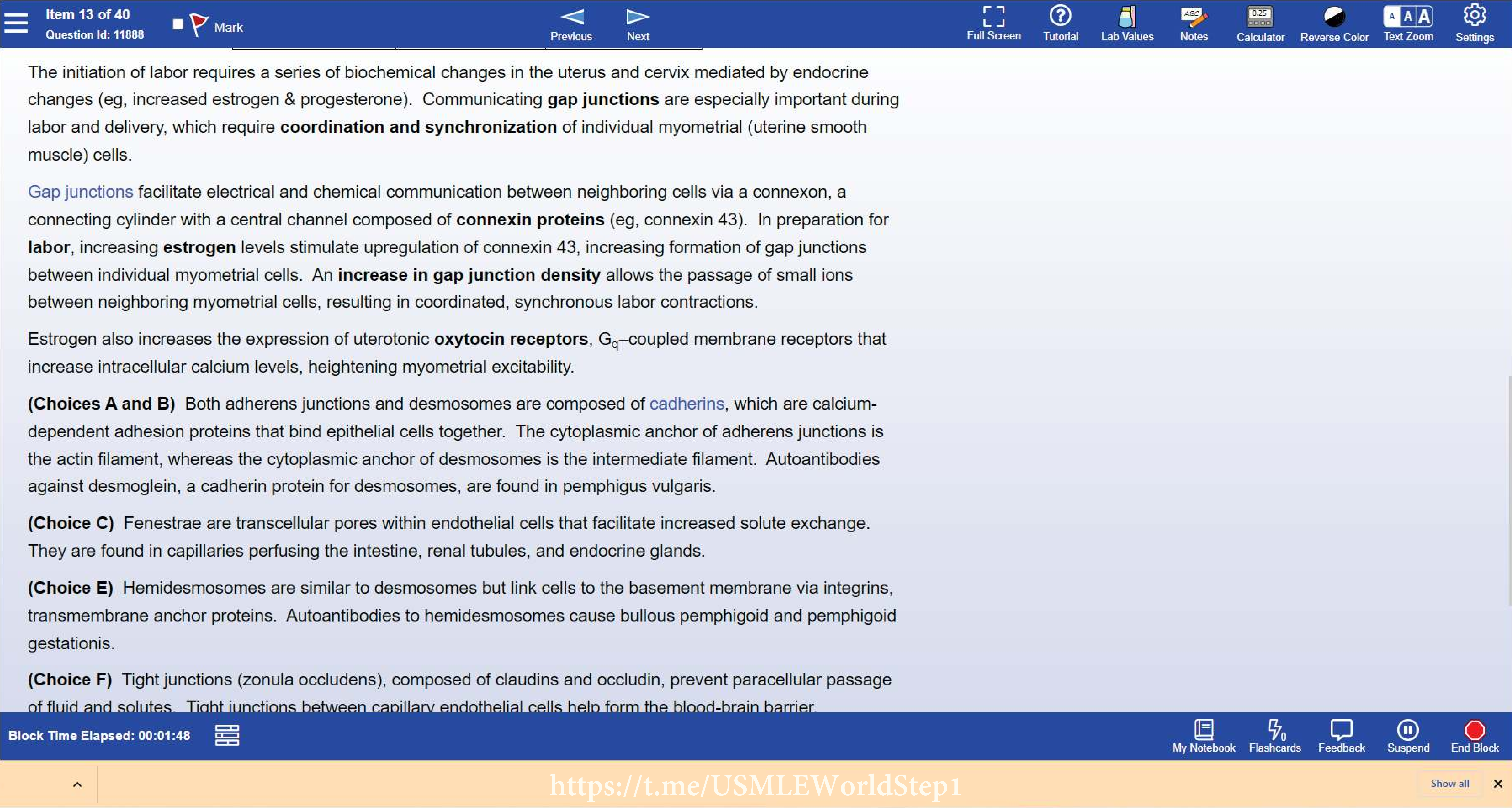
Cell junctions

Type	Proteins	Function
Gap junction	Connexins	Intercellular communication
Tight junction	Claudins, occludin	Paracellular barrier
Adherens junction	Cadherins	Cellular anchor
Desmosomes	Cadherins (eg, desmogleins, desmoplakin)	
Hemidesmosomes	Integrins	

The initiation of labor requires a series of biochemical changes in the uterus and cervix mediated by endocrine changes (eg, increased estrogen & progesterone). Communicating **gap junctions** are especially important during labor and delivery, which require **coordination and synchronization** of individual myometrial (uterine smooth muscle) cells.

Gap junctions facilitate electrical and chemical communication between neighboring cells via a connexon, a connecting cylinder with a central channel composed of **connexin proteins** (eg, connexin 43). In preparation for **labor**, increasing **estrogen** levels stimulate upregulation of connexin 43, increasing formation of gap junctions between individual myometrial cells. An **increase in gap junction density** allows the passage of small ions between neighboring myometrial cells, resulting in coordinated, synchronous labor contractions.

Estrogen also increases the expression of uterotonic **oxytocin receptors**, G_q–coupled membrane receptors that



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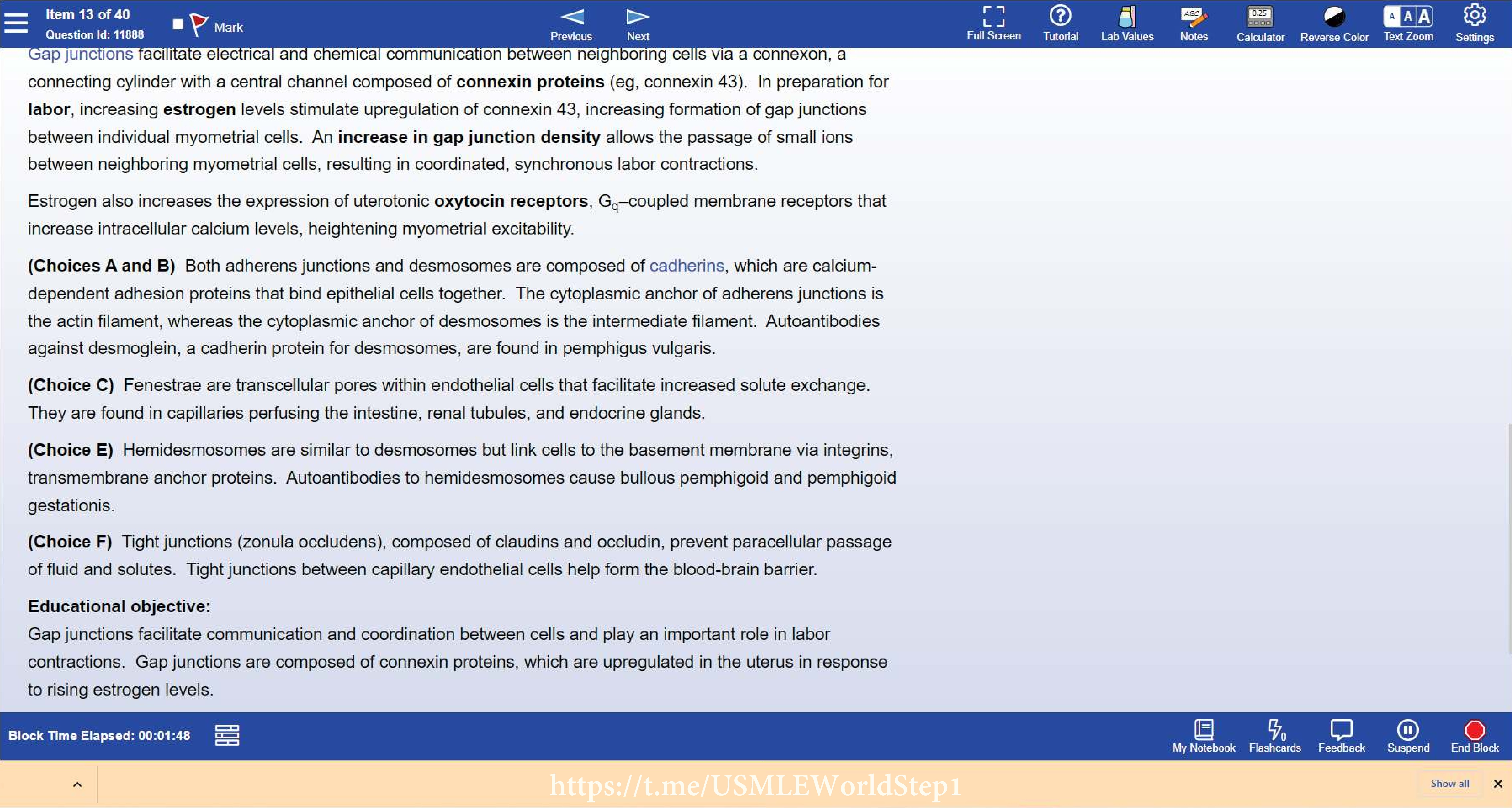
Estrogen also increases the expression of uterotonic **oxytocin receptors**, G_q–coupled membrane receptors that increase intracellular calcium levels, heightening myometrial excitability.

(Choices A and B) Both adherens junctions and desmosomes are composed of cadherins, which are calcium-dependent adhesion proteins that bind epithelial cells together. The cytoplasmic anchor of adherens junctions is the actin filament, whereas the cytoplasmic anchor of desmosomes is the intermediate filament. Autoantibodies against desmoglein, a cadherin protein for desmosomes, are found in pemphigus vulgaris.

(Choice C) Fenestrae are transcellular pores within endothelial cells that facilitate increased solute exchange. They are found in capillaries perfusing the intestine, renal tubules, and endocrine glands.

(Choice E) Hemidesmosomes are similar to desmosomes but link cells to the basement membrane via integrins, transmembrane anchor proteins. Autoantibodies to hemidesmosomes cause bullous pemphigoid and pemphigoid gestationis.

(Choice F) Tight junctions (zonula occludens), composed of claudins and occludin, prevent paracellular passage of fluid and solutes. Tight junctions between capillary endothelial cells help form the blood-brain barrier.



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Educational objective:
Gap junctions facilitate communication and coordination between cells and play an important role in labor contractions. Gap junctions are composed of connexin proteins, which are upregulated in the uterus in response to rising estrogen levels.

Cadherins

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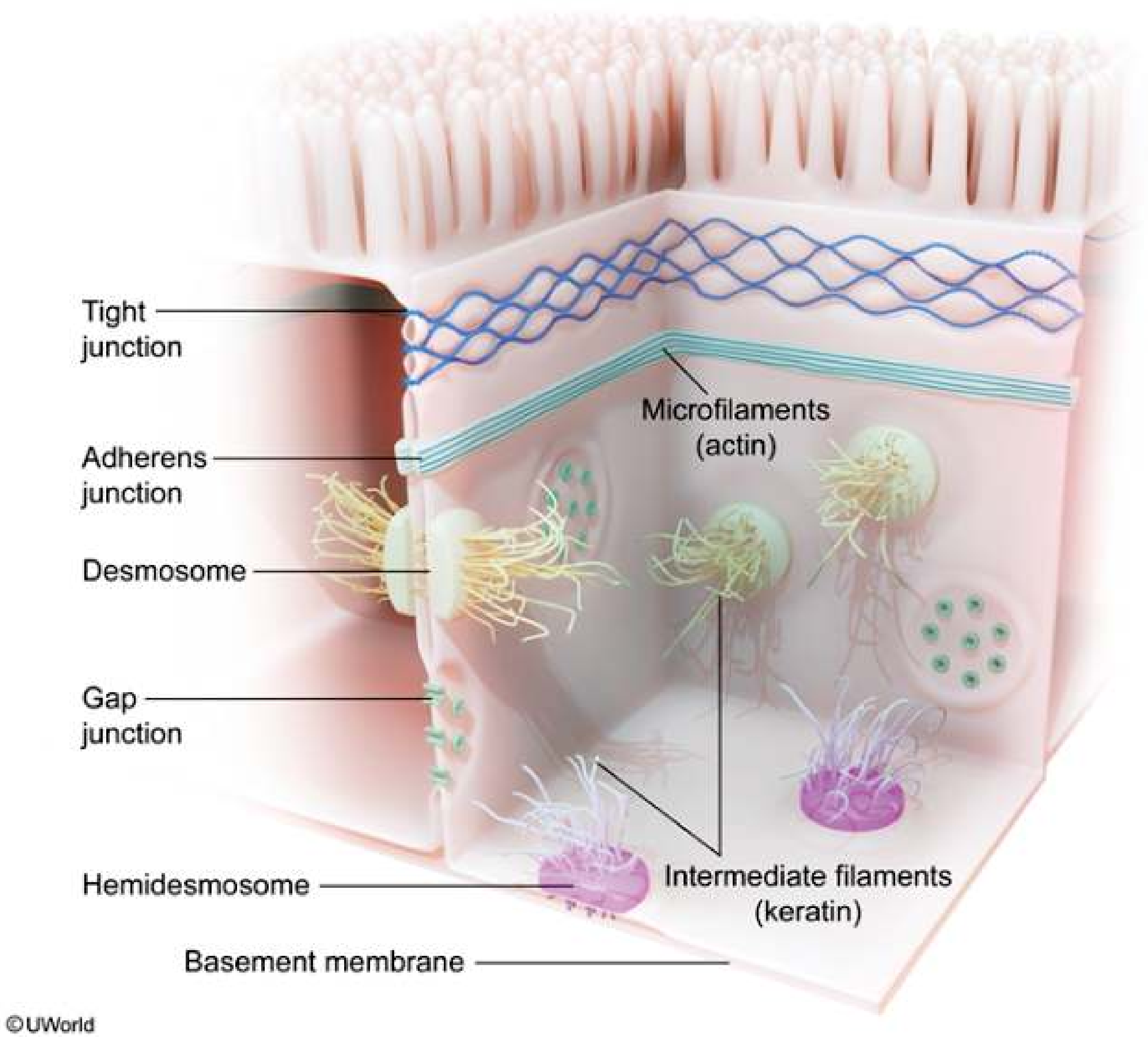
Cell junctions


Tight junction
Adherens junction
Desmosome
Gap junction
Hemidesmosome
Basement membrane
Microfilaments (actin)
Intermediate filaments (keratin)
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(Choice E) Hemidesmosomes are similar to desmosomes but link cells to the basement membrane via integrins,

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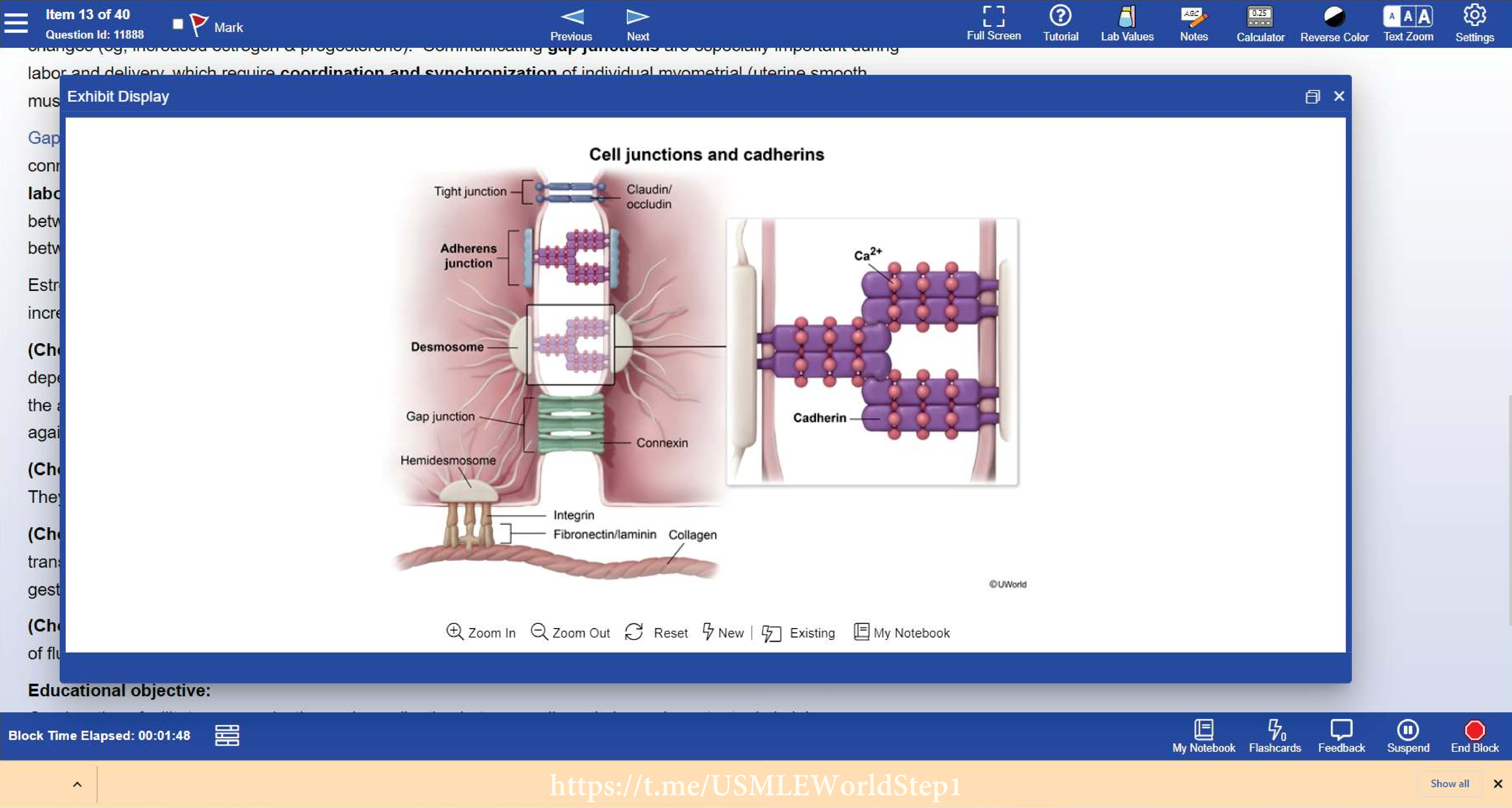
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Tight junction
Claudin/ occludin
Adherens junction
Desmosome
Gap junction
Connexin
Hemidesmosome
Integrin
Fibronectin/laminin
Collagen
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Cadherin
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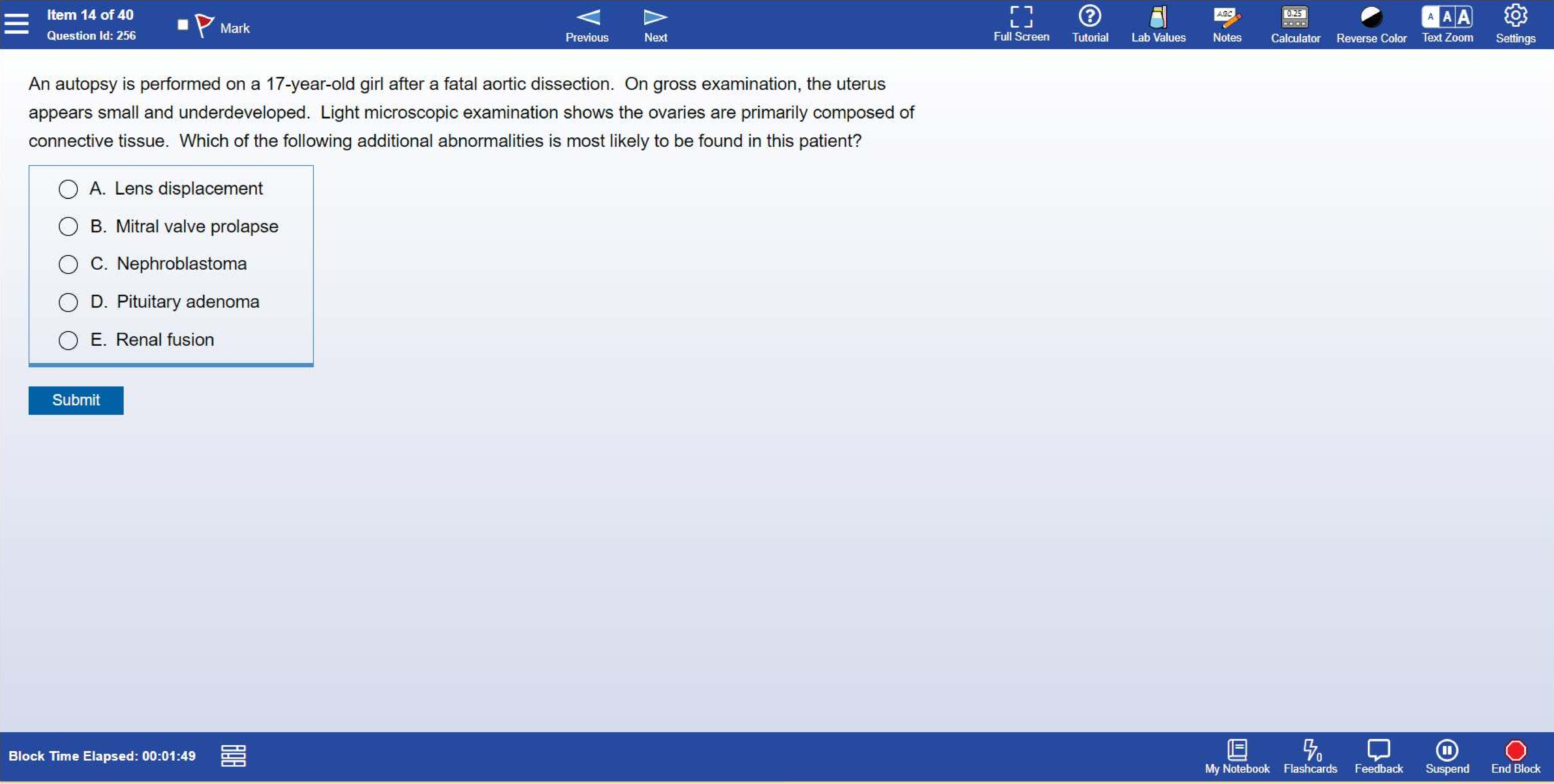
Educational objective:

Cell junctions and cadherins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An autopsy is performed on a 17-year-old girl after a fatal aortic dissection. On gross examination, the uterus appears small and underdeveloped. Light microscopic examination shows the ovaries are primarily composed of connective tissue. Which of the following additional abnormalities is most likely to be found in this patient?

○ A. Lens displacement
○ B. Mitral valve prolapse
○ C. Nephroblastoma
○ D. Pituitary adenoma
○ E. Renal fusion

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- ○ A. Lens displacement (18%)
- ✗ ● B. Mitral valve prolapse (26%)
- ○ C. Nephroblastoma (3%)
- ○ D. Pituitary adenoma (4%)
- ✓ ○ E. Renal fusion (47%)

Incorrect
Correct answer
E

47%
Answered correctly

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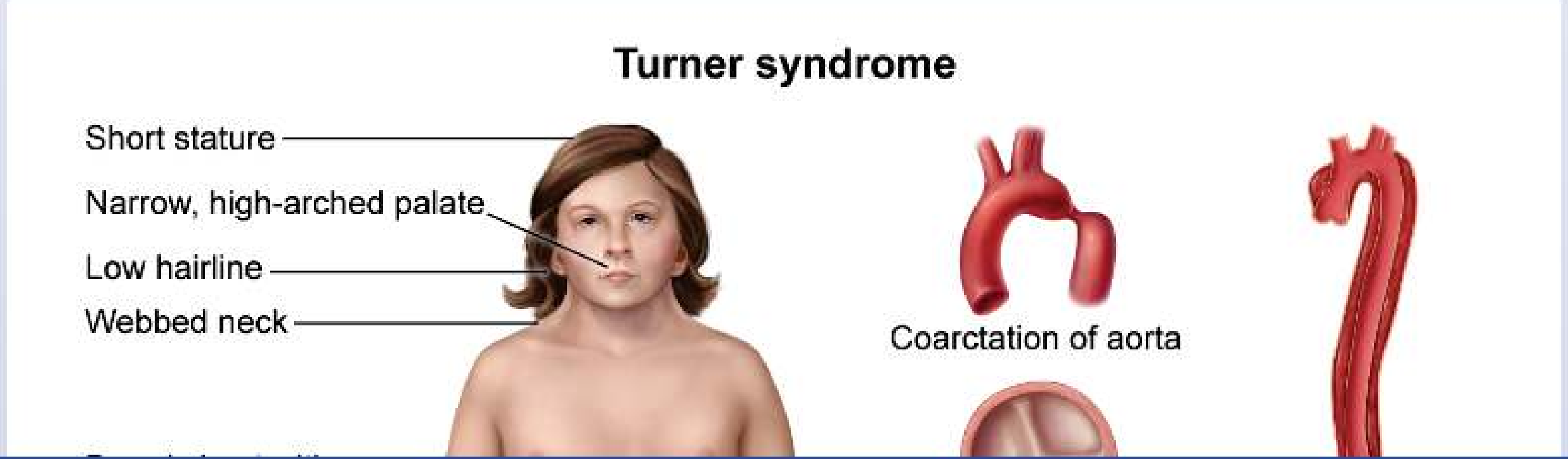
Explanation


Turner syndrome
Short stature
Narrow, high-arched palate
Low hairline
Webbed neck
Coarctation of aorta

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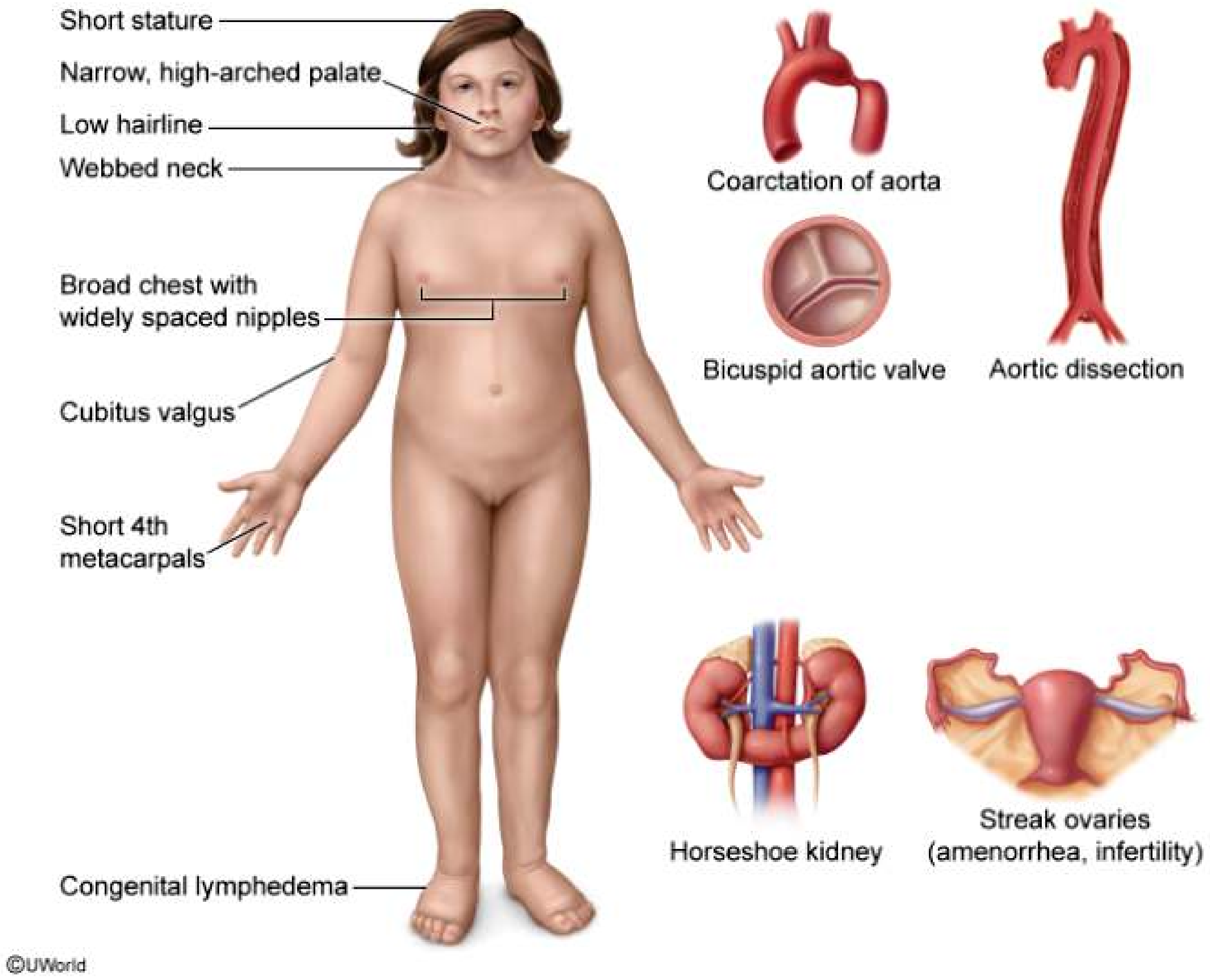
Turner syndrome


Short stature
Narrow, high-arched palate
Low hairline
Webbed neck
Broad chest with widely spaced nipples
Cubitus valgus
Short 4th metacarpals
Congenital lymphedema
Coarctation of aorta
Bicuspid aortic valve
Aortic dissection
Horseshoe kidney
Streak ovaries (amenorrhea, infertility)
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This adolescent girl who died as a result of aortic dissection also had **gonadal dysgenesis**, a finding that suggests **Turner syndrome** (TS). TS is due to loss of an X chromosome (45,X) and is the most common cause of ovarian dysgenesis.

During early gestation, ovarian development is initially normal in TS. However, germ cells subsequently undergo accelerated apoptosis, and ovarian follicles are replaced by connective tissue (ie, **streak ovaries**), resulting in **primary ovarian insufficiency**. At puberty, girls with TS may develop pubic hair (due to normal adrenal androgen production) but typically have absent breast development and primary amenorrhea due to lack of ovarian estrogen production. Growth and maturation of the uterus are also estrogen dependent, as seen in this girl with a small and underdeveloped uterus; most patients are infertile.

Extragonadal manifestations of TS include but are not limited to:

- Physical features: Short stature, broad chest, and webbed neck are characteristic.
- Cardiac anomalies: Bicuspid aortic valve and aortic coarctation are the most common, and patients are at increased risk for **aortic dissection** at a young age, as seen here.
- Renal anomalies: These occur in almost half of patients and include collecting system malformations (eg, ureter duplication) and **horseshoe kidney** (fusion of the lower renal poles). Although horseshoe kidney can lead to recurrent urinary tract infections, it is often asymptomatic and may go undetected.

(Choices A and B) Lens displacement and mitral valve prolapse are seen in Marfan syndrome. Patients with Marfan syndrome are at risk for aortic dissection but do not have streak ovaries or an underdeveloped uterus.

(Choice C) Nephroblastoma (Wilms tumor) is the most common renal malignancy in children and is associated with WAGR syndrome (**W**ilms tumor, **A**niridia, **G**enitourinary anomalies, and **R**ange of developmental delays). Girls with this condition can have streak gonads but are not at increased risk for aortic dissection. In addition,

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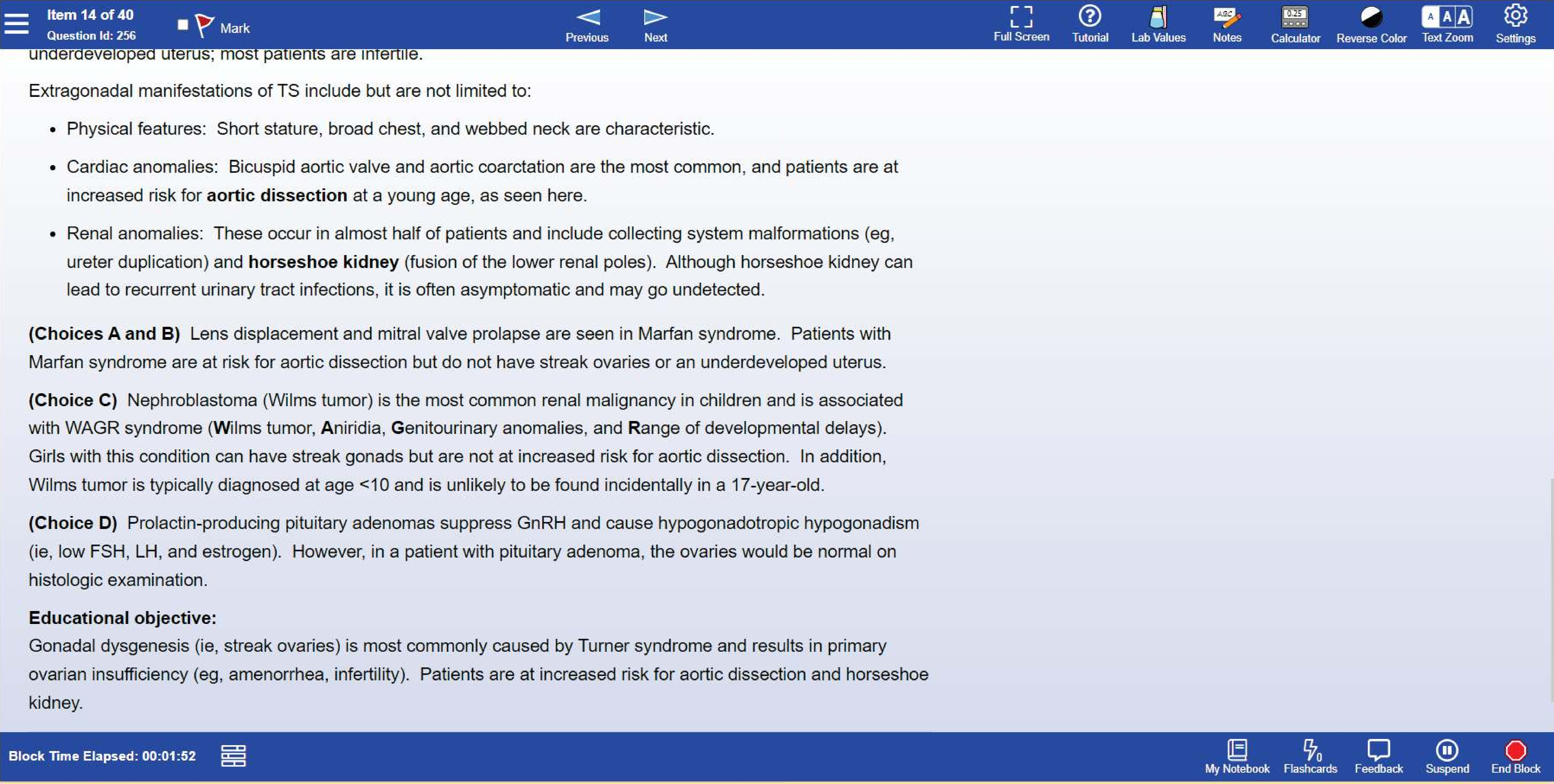
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Extragonadal manifestations of TS include but are not limited to:

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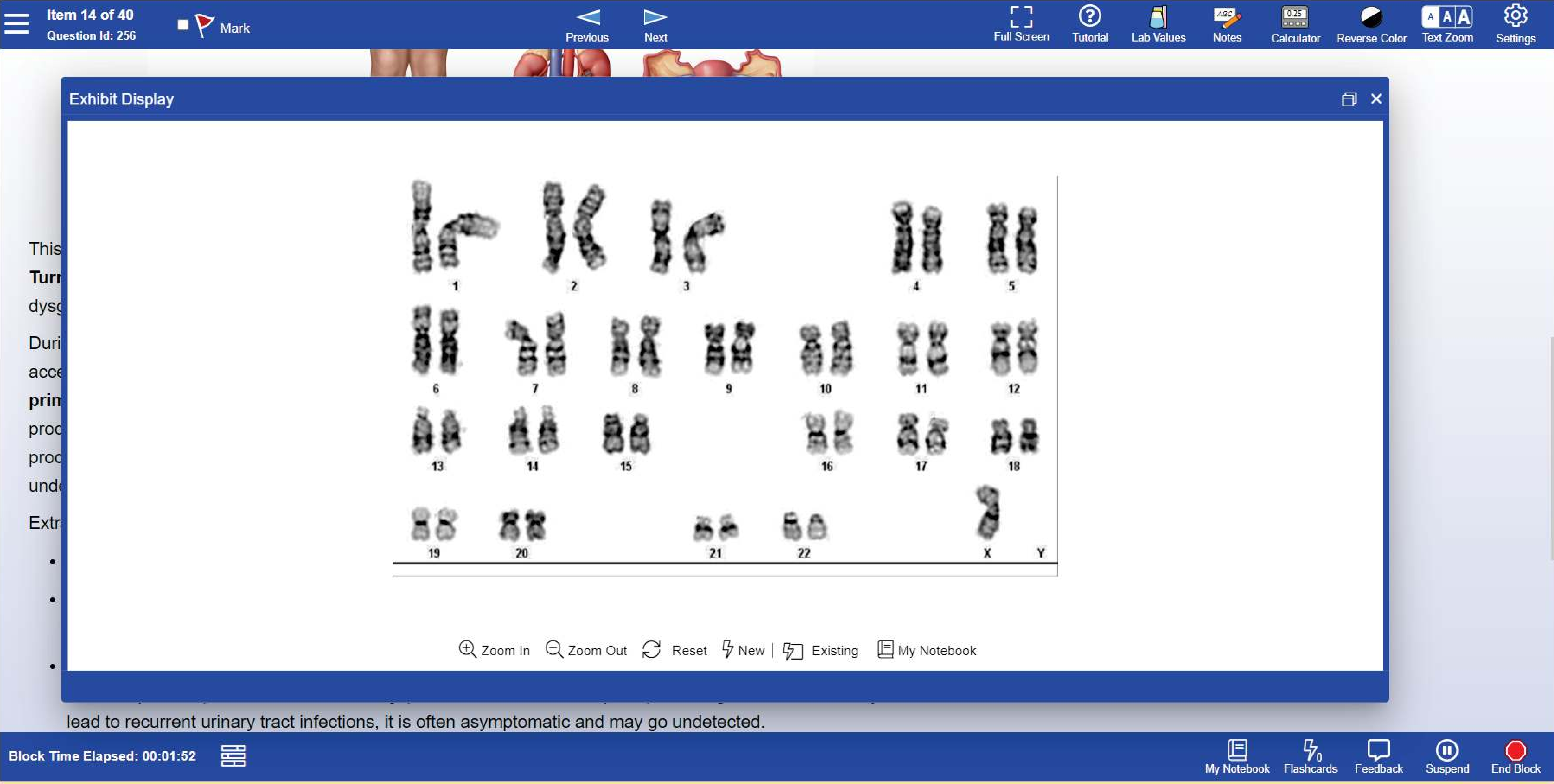
(Choice D) Prolactin-producing pituitary adenomas suppress GnRH and cause hypogonadotropic hypogonadism (ie, low FSH, LH, and estrogen). However, in a patient with pituitary adenoma, the ovaries would be normal on histologic examination.

Educational objective:

Gonadal dysgenesis (ie, streak ovaries) is most commonly caused by Turner syndrome and results in primary ovarian insufficiency (eg, amenorrhea, infertility). Patients are at increased risk for aortic dissection and horseshoe kidney.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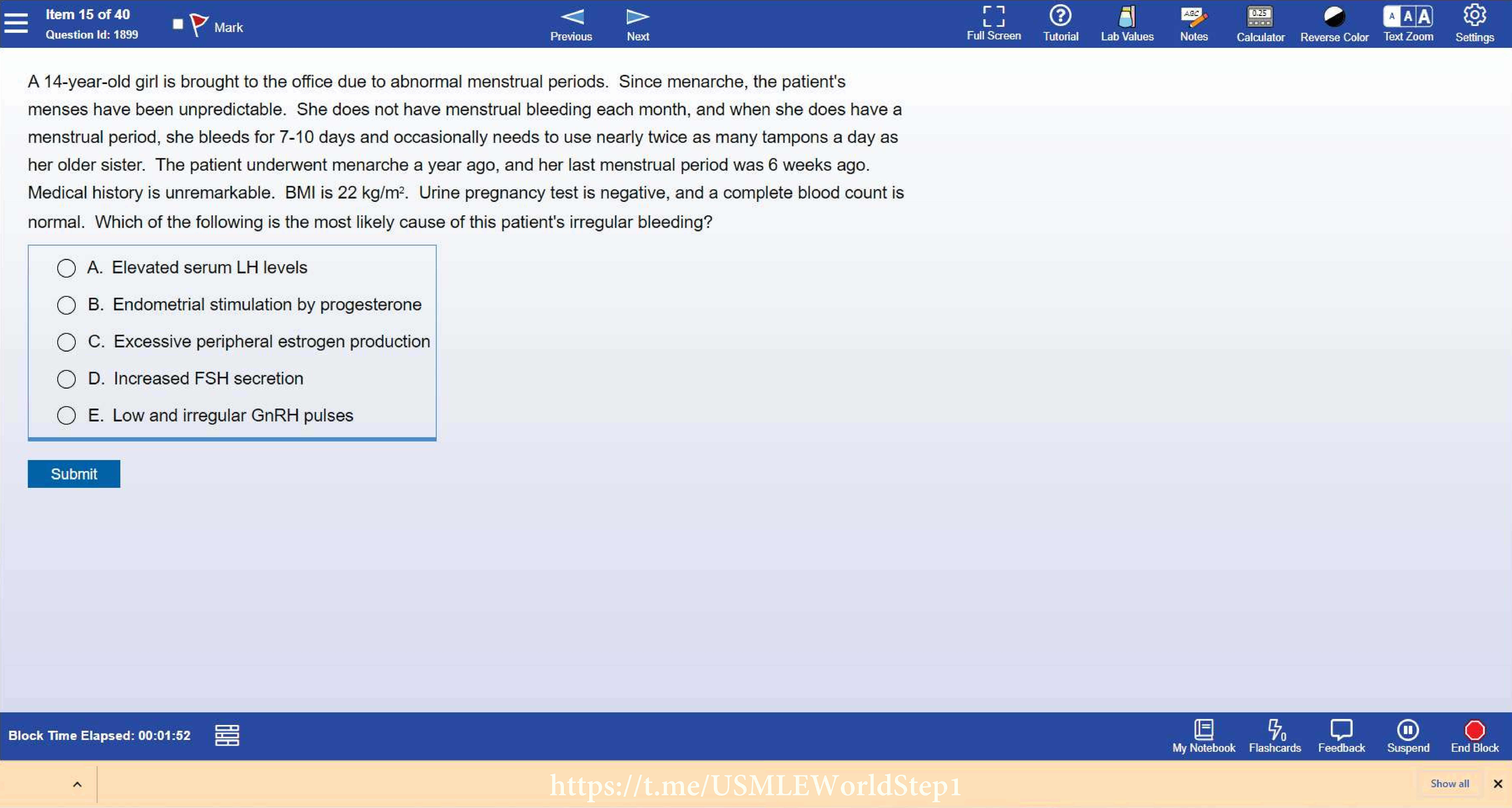
lead to recurrent urinary tract infections, it is often asymptomatic and may go undetected.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A 14-year-old girl is brought to the office due to abnormal menstrual periods. Since menarche, the patient's menses have been unpredictable. She does not have menstrual bleeding each month, and when she does have a menstrual period, she bleeds for 7-10 days and occasionally needs to use nearly twice as many tampons a day as her older sister. The patient underwent menarche a year ago, and her last menstrual period was 6 weeks ago. Medical history is unremarkable. BMI is 22 kg/m^2. Urine pregnancy test is negative, and a complete blood count is normal. Which of the following is the most likely cause of this patient's irregular bleeding?

- ○ A. Elevated serum LH levels
- ○ B. Endometrial stimulation by progesterone
- ○ C. Excessive peripheral estrogen production
- ○ D. Increased FSH secretion
- ○ E. Low and irregular GnRH pulses

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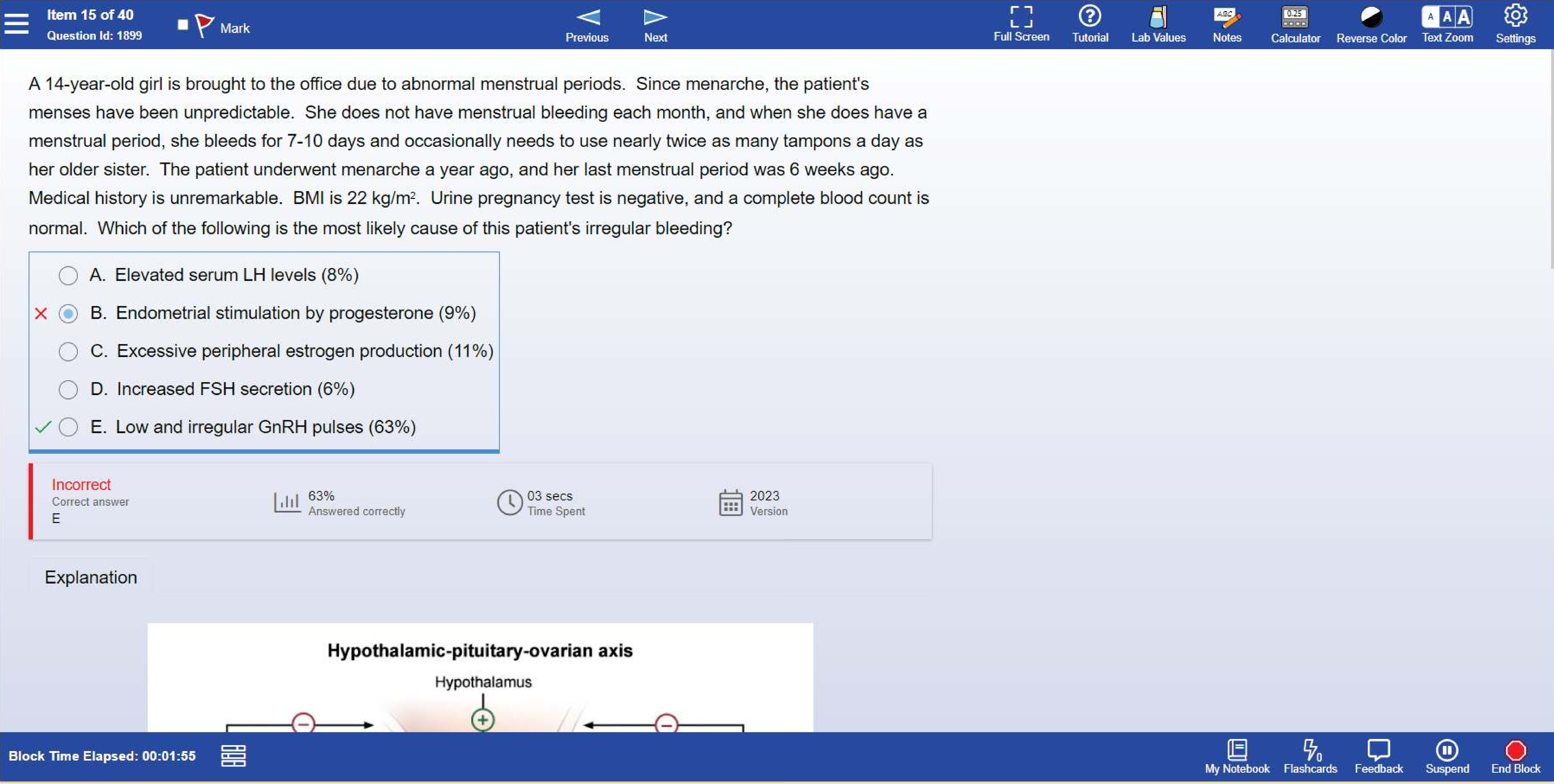
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- ○ A. Elevated serum LH levels (8%)
- ✗ ● B. Endometrial stimulation by progesterone (9%)
- ○ C. Excessive peripheral estrogen production (11%)
- ○ D. Increased FSH secretion (6%)
- ✓ ○ E. Low and irregular GnRH pulses (63%)

Incorrect
Correct answer
E

63%
Answered correctly

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Explanation

Hypothalamic-pituitary-ovarian axis

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✓ ○ E. Low and irregular GnRH pulses (63%)

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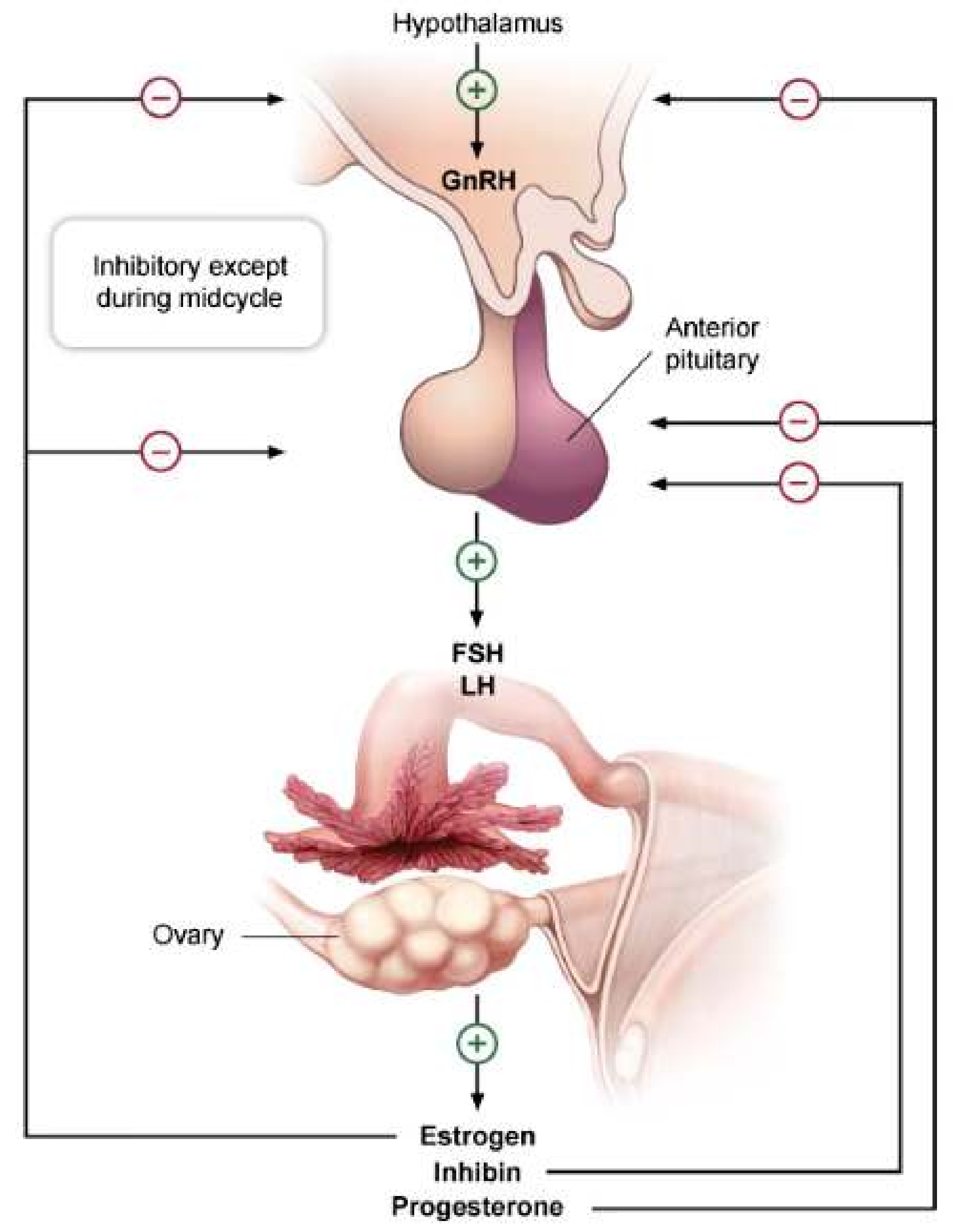
Hypothalamic-pituitary-ovarian axis



Hypothalamus
GnRH
Inhibitory except during midcycle
Anterior pituitary
FSH
LH
Ovary
Estrogen
Inhibin
Progesterone

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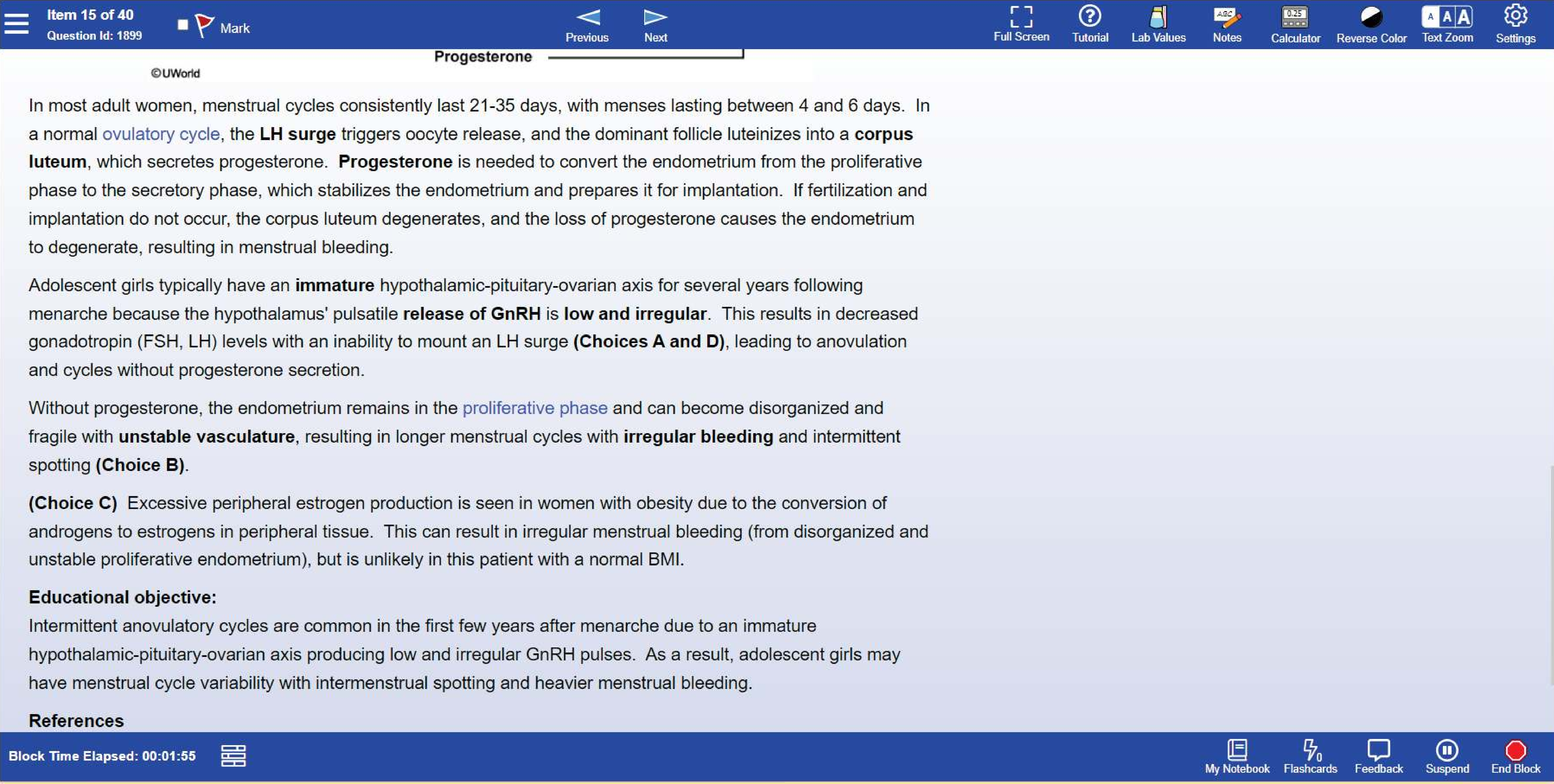
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In most adult women, menstrual cycles consistently last 21-35 days, with menses lasting between 4 and 6 days. In a normal ovulatory cycle, the **LH surge** triggers oocyte release, and the dominant follicle luteinizes into a **corpus luteum**, which secretes progesterone. **Progesterone** is needed to convert the endometrium from the proliferative phase to the secretory phase, which stabilizes the endometrium and prepares it for implantation. If fertilization and implantation do not occur, the corpus luteum degenerates, and the loss of progesterone causes the endometrium to degenerate, resulting in menstrual bleeding.

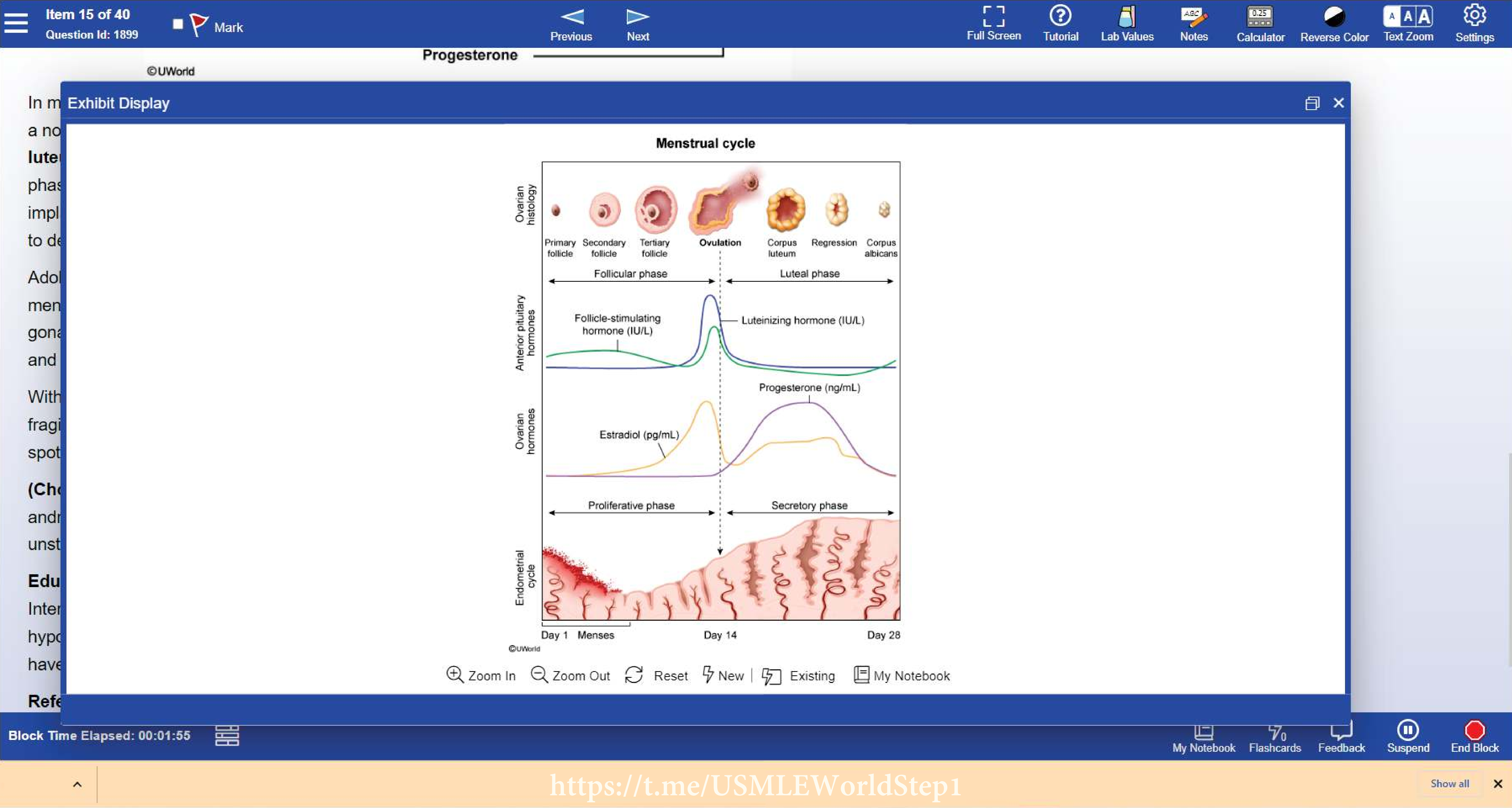
Adolescent girls typically have an **immature** hypothalamic-pituitary-ovarian axis for several years following menarche because the hypothalamus' pulsatile **release of GnRH** is **low and irregular**. This results in decreased gonadotropin (FSH, LH) levels with an inability to mount an LH surge **(Choices A and D)**, leading to anovulation and cycles without progesterone secretion.

Without progesterone, the endometrium remains in the proliferative phase and can become disorganized and fragile with **unstable vasculature**, resulting in longer menstrual cycles with **irregular bleeding** and intermittent spotting **(Choice B)**.

(Choice C) Excessive peripheral estrogen production is seen in women with obesity due to the conversion of androgens to estrogens in peripheral tissue. This can result in irregular menstrual bleeding (from disorganized and unstable proliferative endometrium), but is unlikely in this patient with a normal BMI.

Educational objective:
Intermittent anovulatory cycles are common in the first few years after menarche due to an immature hypothalamic-pituitary-ovarian axis producing low and irregular GnRH pulses. As a result, adolescent girls may have menstrual cycle variability with intermenstrual spotting and heavier menstrual bleeding.

References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Menstrual cycle
Ovarian histology
Primary follicle
Secondary follicle
Tertiary follicle
Ovulation
Corpus luteum
Regression
Corpus albicans
Follicular phase
Luteal phase
Anterior pituitary hormones
Follicle-stimulating hormone (IU/L)
Luteinizing hormone (IU/L)
Ovarian hormones
Progesterone (ng/mL)
Estradiol (pg/mL)
Proliferative phase
Secretory phase
Endometrial cycle
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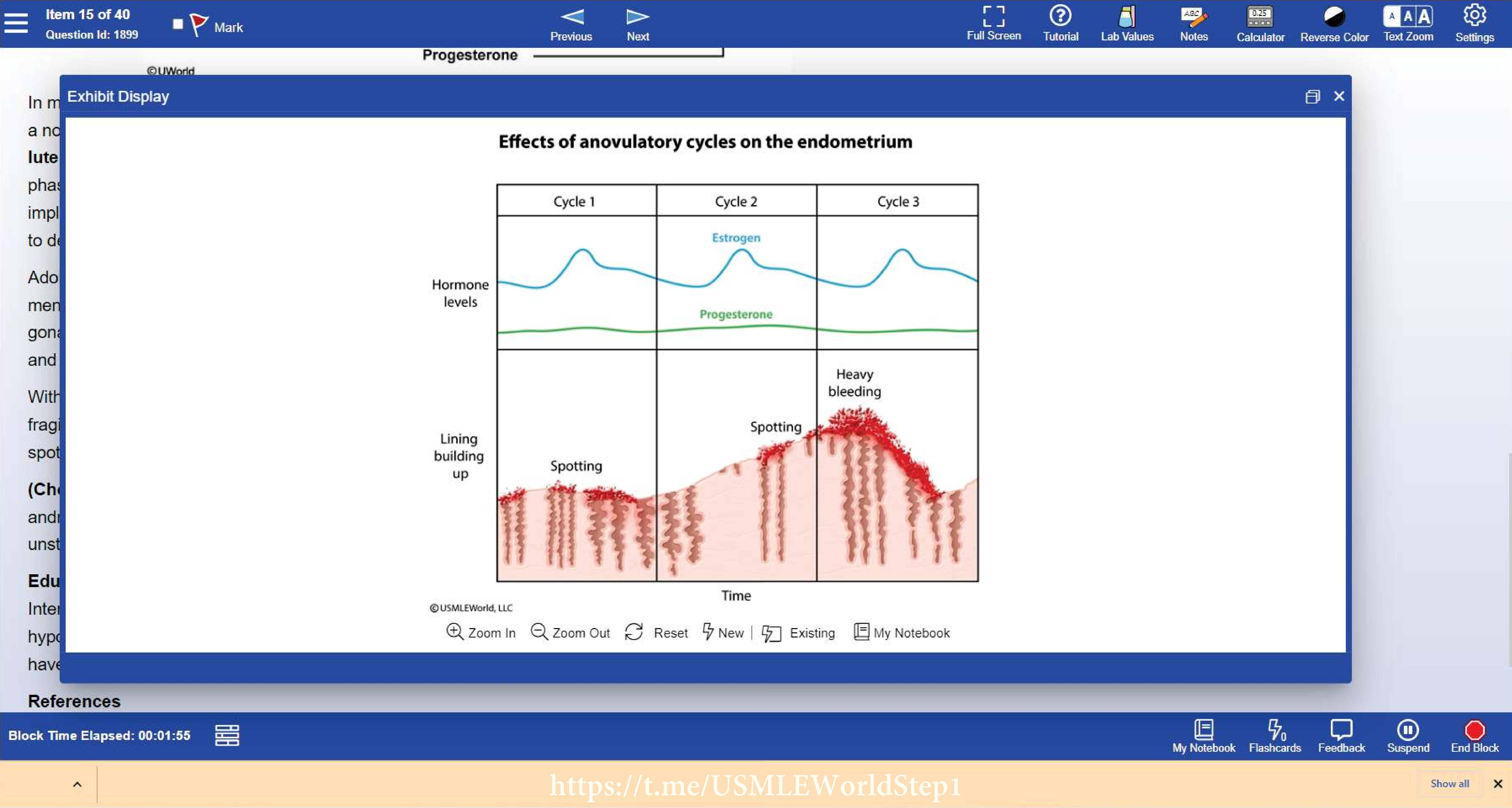
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Effects of anovulatory cycles on the endometrium

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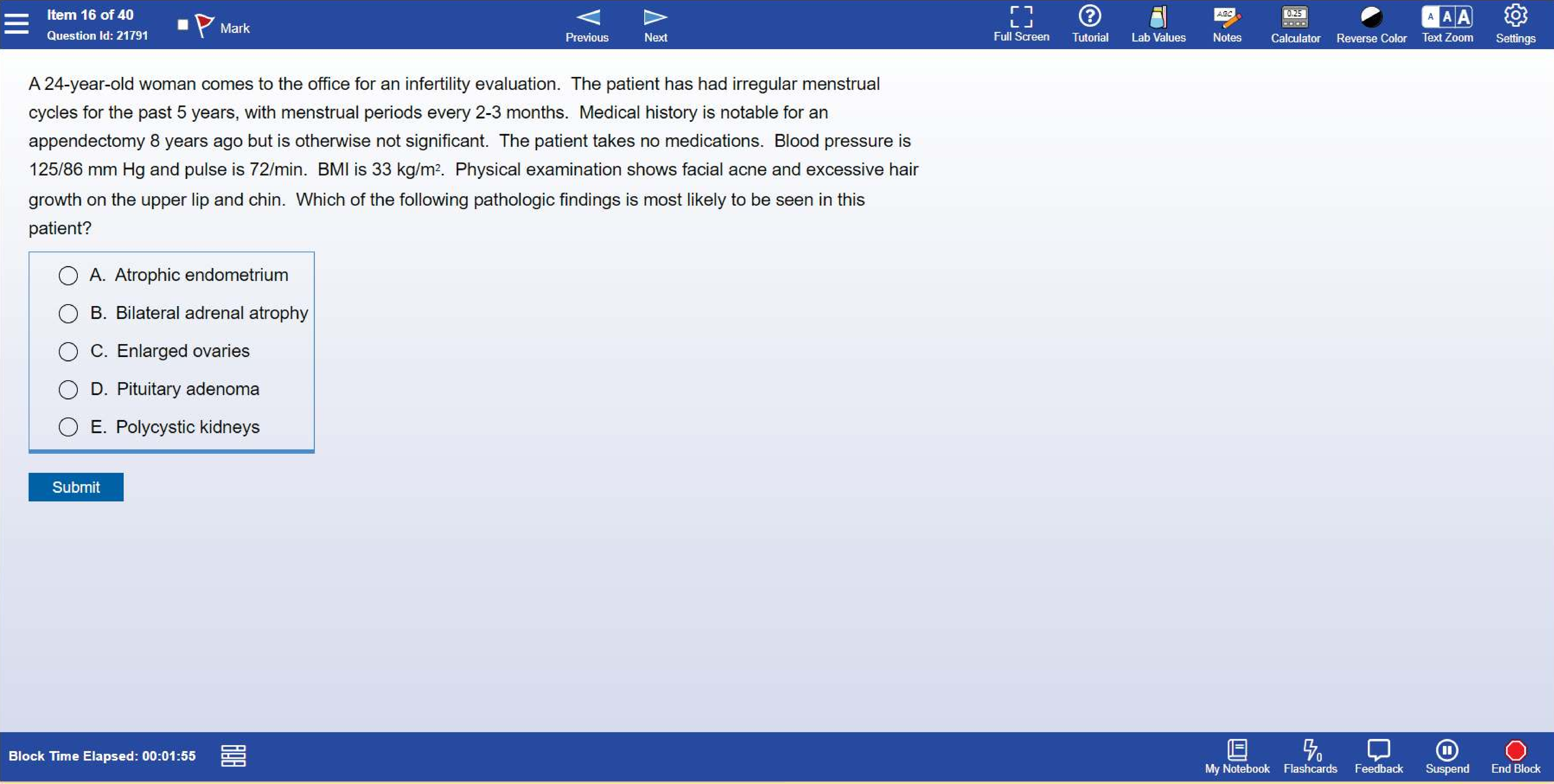
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A 24-year-old woman comes to the office for an infertility evaluation. The patient has had irregular menstrual cycles for the past 5 years, with menstrual periods every 2-3 months. Medical history is notable for an appendectomy 8 years ago but is otherwise not significant. The patient takes no medications. Blood pressure is 125/86 mm Hg and pulse is 72/min. BMI is 33 kg/m^2. Physical examination shows facial acne and excessive hair growth on the upper lip and chin. Which of the following pathologic findings is most likely to be seen in this patient?

○ A. Atrophic endometrium
○ B. Bilateral adrenal atrophy
○ C. Enlarged ovaries
○ D. Pituitary adenoma
○ E. Polycystic kidneys

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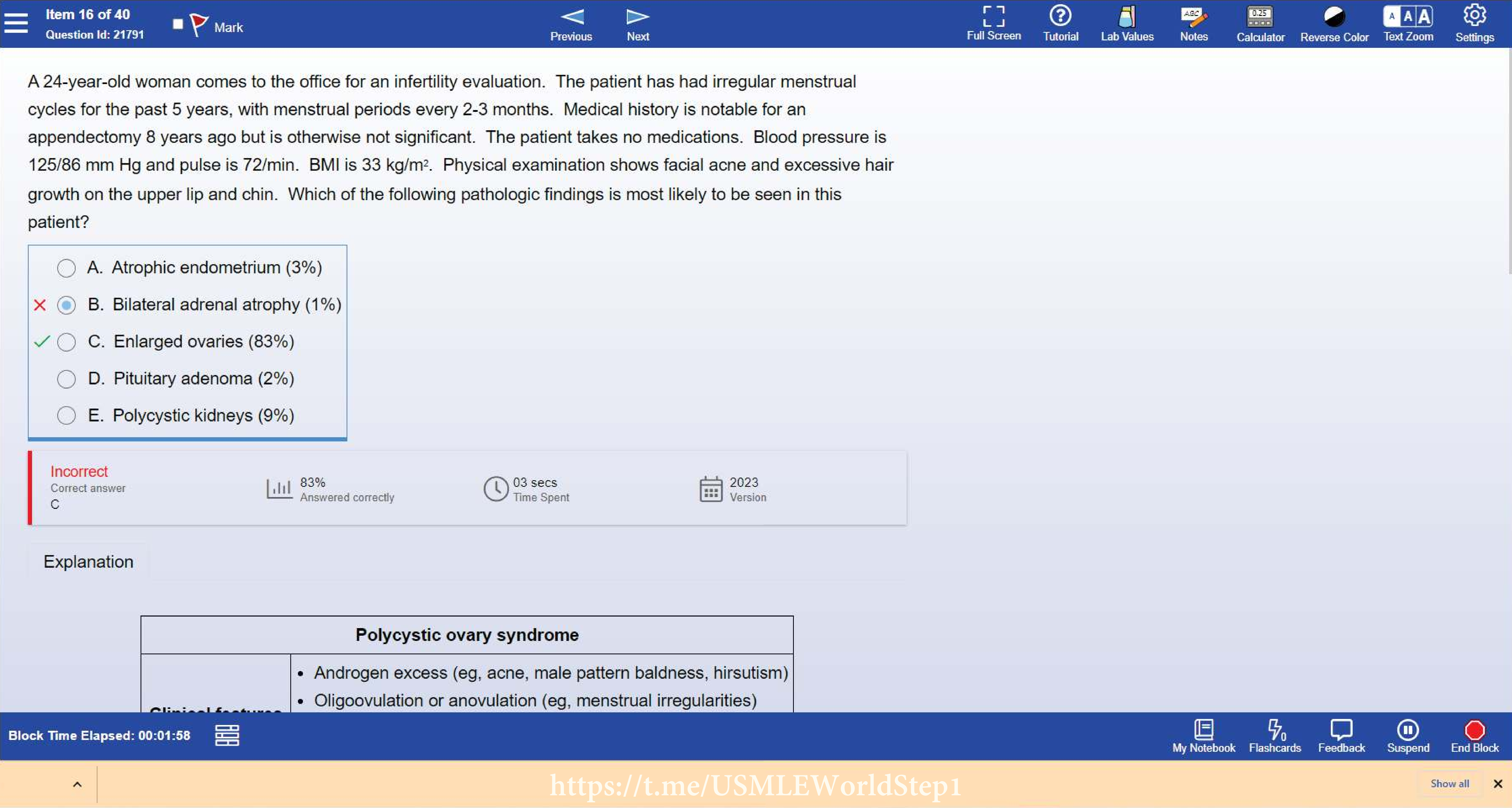
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- ○ A. Atrophic endometrium (3%)
- ✗ ● B. Bilateral adrenal atrophy (1%)
- ✓ ○ C. Enlarged ovaries (83%)
- ○ D. Pituitary adenoma (2%)
- ○ E. Polycystic kidneys (9%)

Incorrect
Correct answer
C

83%
Answered correctly

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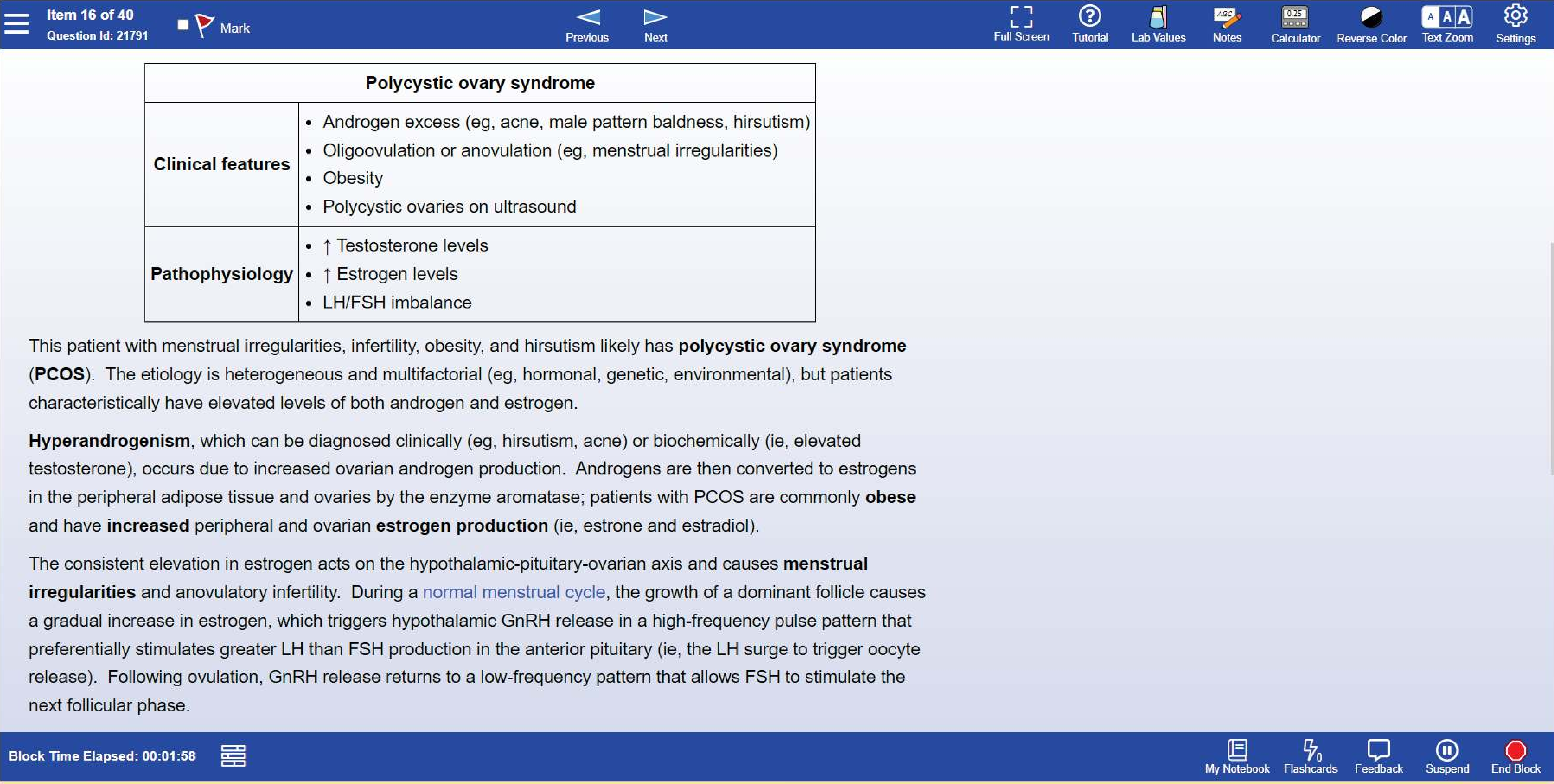
Explanation

Polycystic ovary syndrome	
Clinical features	• Androgen excess (eg, acne, male pattern baldness, hirsutism) • Oligoovulation or anovulation (eg, menstrual irregularities)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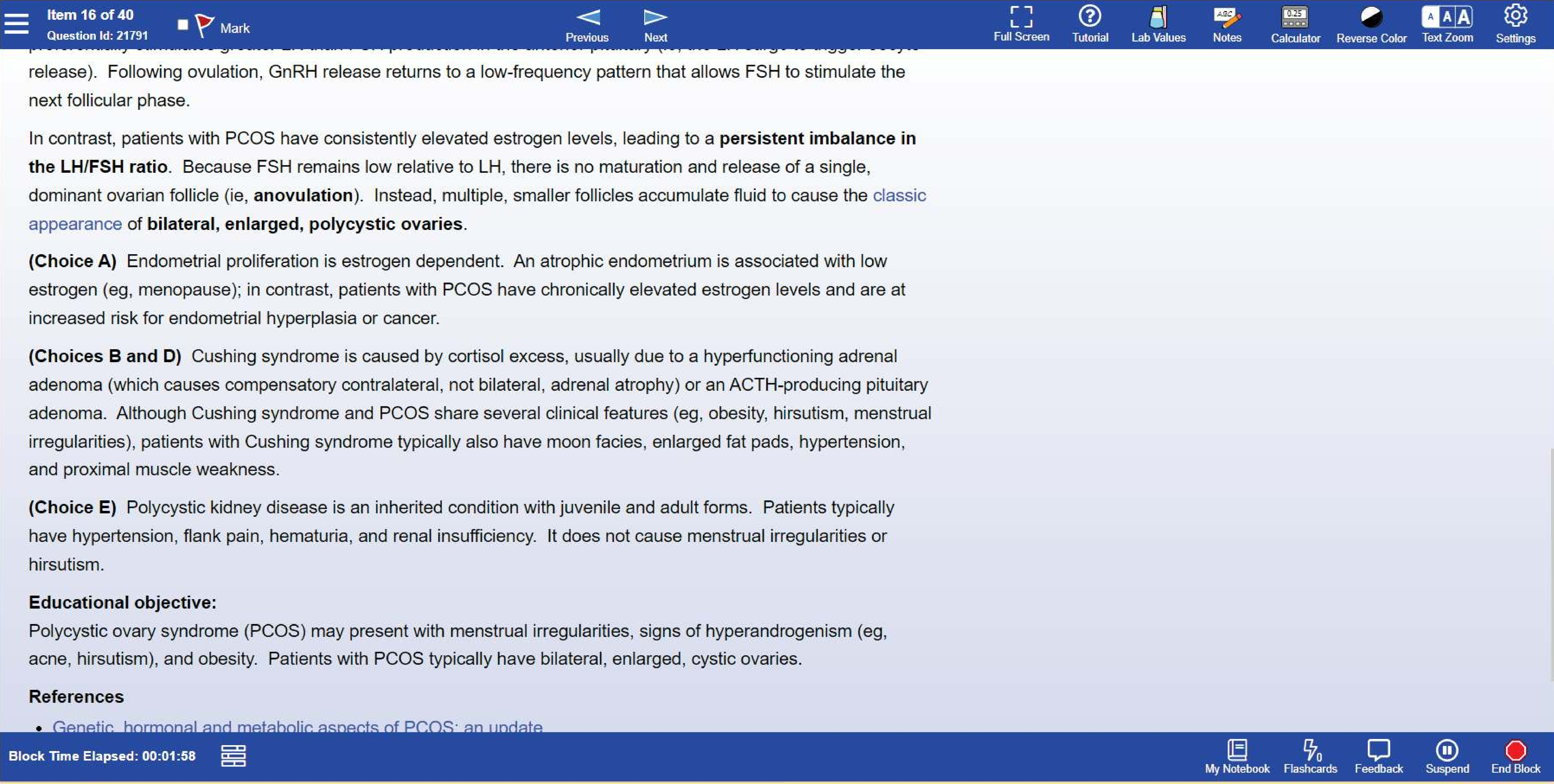
Polycystic ovary syndrome	
Clinical features	• Androgen excess (eg, acne, male pattern baldness, hirsutism) • Oligoovulation or anovulation (eg, menstrual irregularities) • Obesity • Polycystic ovaries on ultrasound
Pathophysiology	• ↑ Testosterone levels • ↑ Estrogen levels • LH/FSH imbalance

This patient with menstrual irregularities, infertility, obesity, and hirsutism likely has **polycystic ovary syndrome** (**PCOS**). The etiology is heterogeneous and multifactorial (eg, hormonal, genetic, environmental), but patients characteristically have elevated levels of both androgen and estrogen.

Hyperandrogenism, which can be diagnosed clinically (eg, hirsutism, acne) or biochemically (ie, elevated testosterone), occurs due to increased ovarian androgen production. Androgens are then converted to estrogens in the peripheral adipose tissue and ovaries by the enzyme aromatase; patients with PCOS are commonly **obese** and have **increased** peripheral and ovarian **estrogen production** (ie, estrone and estradiol).

The consistent elevation in estrogen acts on the hypothalamic-pituitary-ovarian axis and causes **menstrual irregularities** and anovulatory infertility. During a normal menstrual cycle, the growth of a dominant follicle causes a gradual increase in estrogen, which triggers hypothalamic GnRH release in a high-frequency pulse pattern that preferentially stimulates greater LH than FSH production in the anterior pituitary (ie, the LH surge to trigger oocyte release). Following ovulation, GnRH release returns to a low-frequency pattern that allows FSH to stimulate the next follicular phase.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release). Following ovulation, GnRH release returns to a low-frequency pattern that allows FSH to stimulate the next follicular phase.

In contrast, patients with PCOS have consistently elevated estrogen levels, leading to a **persistent imbalance in the LH/FSH ratio**. Because FSH remains low relative to LH, there is no maturation and release of a single, dominant ovarian follicle (ie, **anovulation**). Instead, multiple, smaller follicles accumulate fluid to cause the classic appearance of **bilateral, enlarged, polycystic ovaries**.

(Choice A) Endometrial proliferation is estrogen dependent. An atrophic endometrium is associated with low estrogen (eg, menopause); in contrast, patients with PCOS have chronically elevated estrogen levels and are at increased risk for endometrial hyperplasia or cancer.

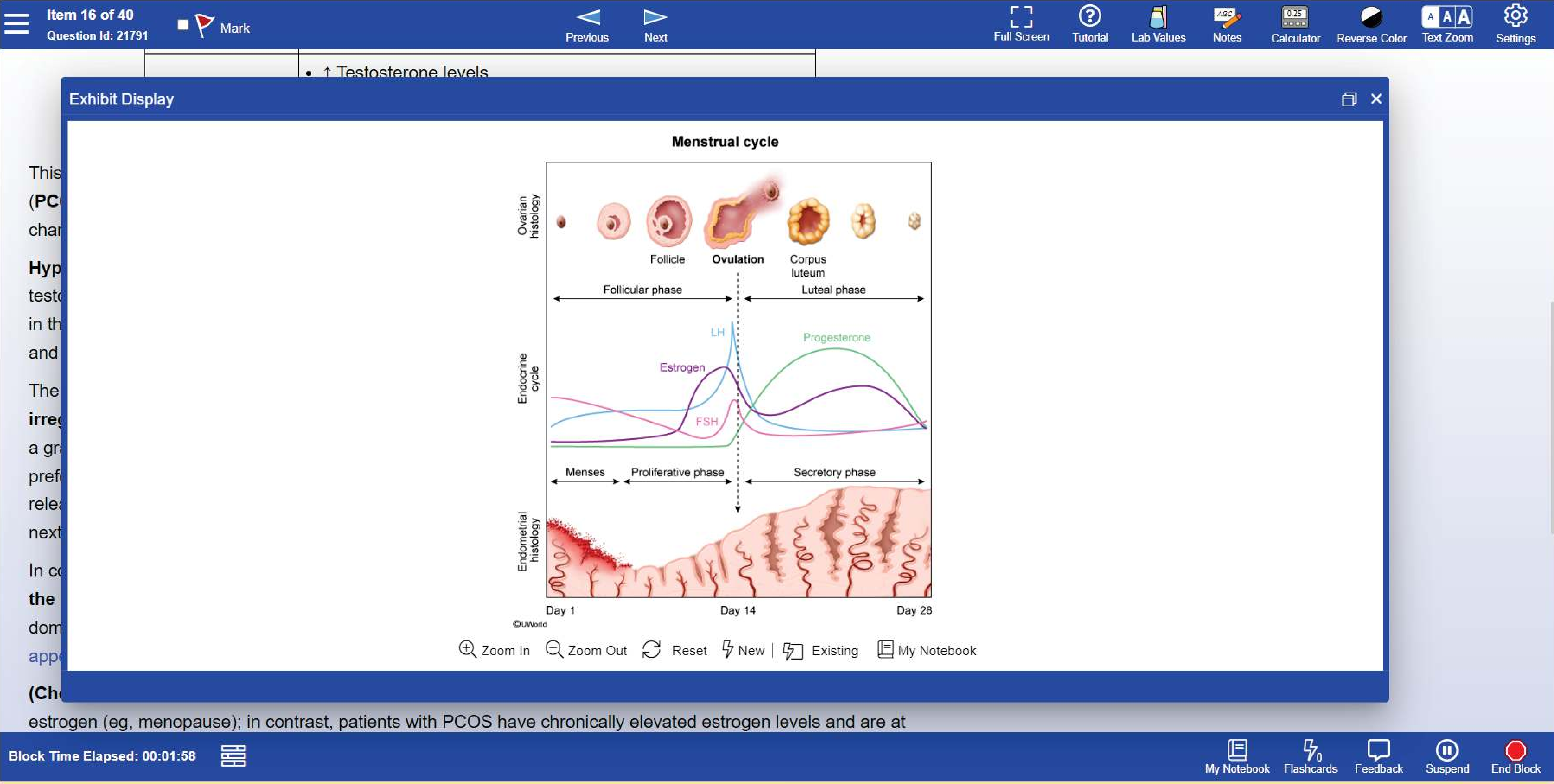
(Choices B and D) Cushing syndrome is caused by cortisol excess, usually due to a hyperfunctioning adrenal adenoma (which causes compensatory contralateral, not bilateral, adrenal atrophy) or an ACTH-producing pituitary adenoma. Although Cushing syndrome and PCOS share several clinical features (eg, obesity, hirsutism, menstrual irregularities), patients with Cushing syndrome typically also have moon facies, enlarged fat pads, hypertension, and proximal muscle weakness.

(Choice E) Polycystic kidney disease is an inherited condition with juvenile and adult forms. Patients typically have hypertension, flank pain, hematuria, and renal insufficiency. It does not cause menstrual irregularities or hirsutism.

Educational objective:
Polycystic ovary syndrome (PCOS) may present with menstrual irregularities, signs of hyperandrogenism (eg, acne, hirsutism), and obesity. Patients with PCOS typically have bilateral, enlarged, cystic ovaries.

References

- Genetic, hormonal and metabolic aspects of PCOS: an update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Follicular phase
Luteal phase
Endocrine cycle
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Estrogen
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Proliferative phase
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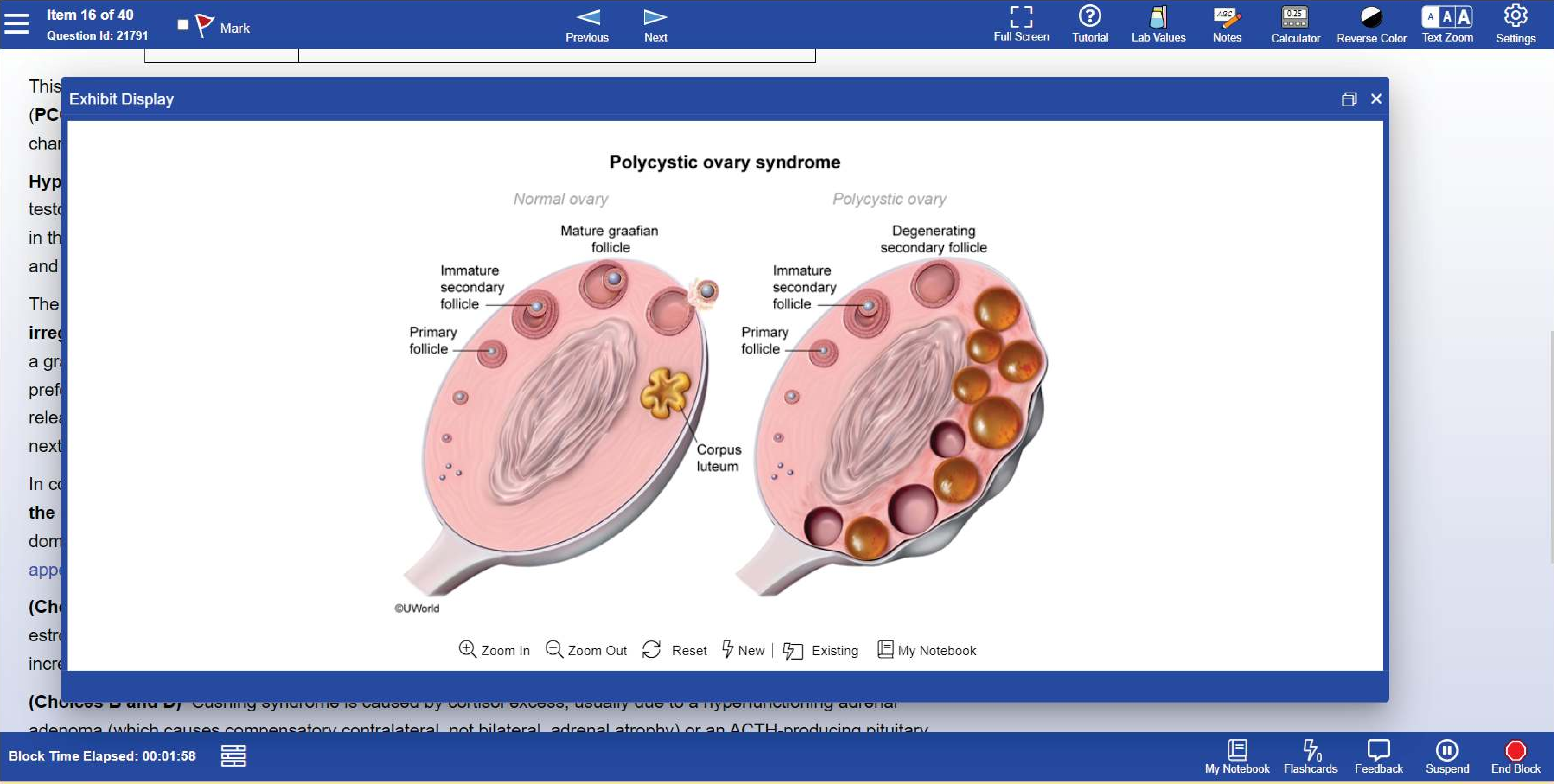
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Polycystic ovary syndrome

Normal ovary
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Immature secondary follicle
Primary follicle
Corpus luteum
Polycystic ovary
Degenerating secondary follicle
Immature secondary follicle
Primary follicle

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(Choices B and D) Cushing syndrome is caused by cortisol excess, usually due to a hyperfunctioning adrenal adenoma (which causes compensatory contralateral, not bilateral, adrenal atrophy) or an ACTH-producing pituitary

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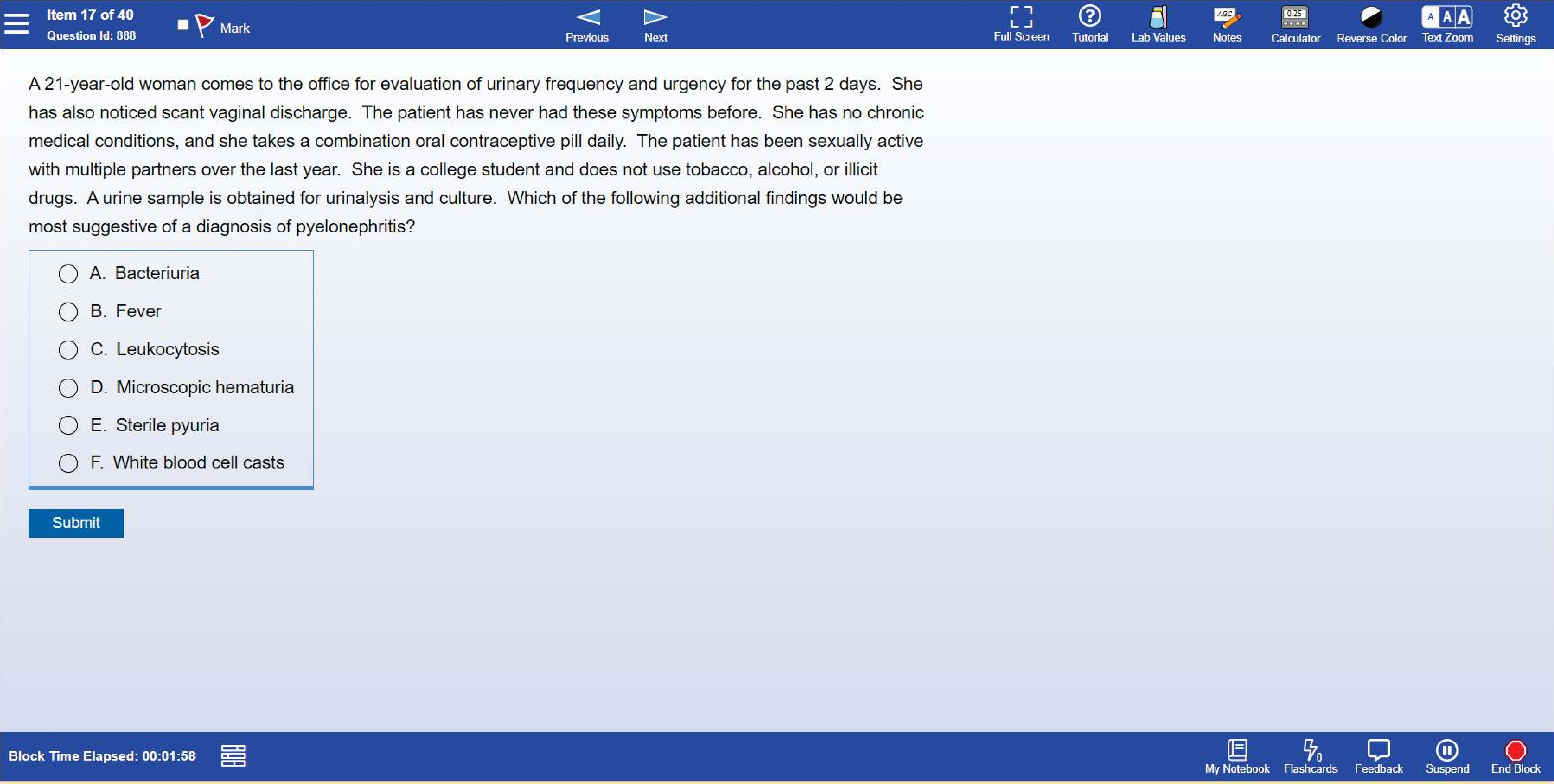
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A 21-year-old woman comes to the office for evaluation of urinary frequency and urgency for the past 2 days. She has also noticed scant vaginal discharge. The patient has never had these symptoms before. She has no chronic medical conditions, and she takes a combination oral contraceptive pill daily. The patient has been sexually active with multiple partners over the last year. She is a college student and does not use tobacco, alcohol, or illicit drugs. A urine sample is obtained for urinalysis and culture. Which of the following additional findings would be most suggestive of a diagnosis of pyelonephritis?

- ○ A. Bacteriuria
- ○ B. Fever
- ○ C. Leukocytosis
- ○ D. Microscopic hematuria
- ○ E. Sterile pyuria
- ○ F. White blood cell casts

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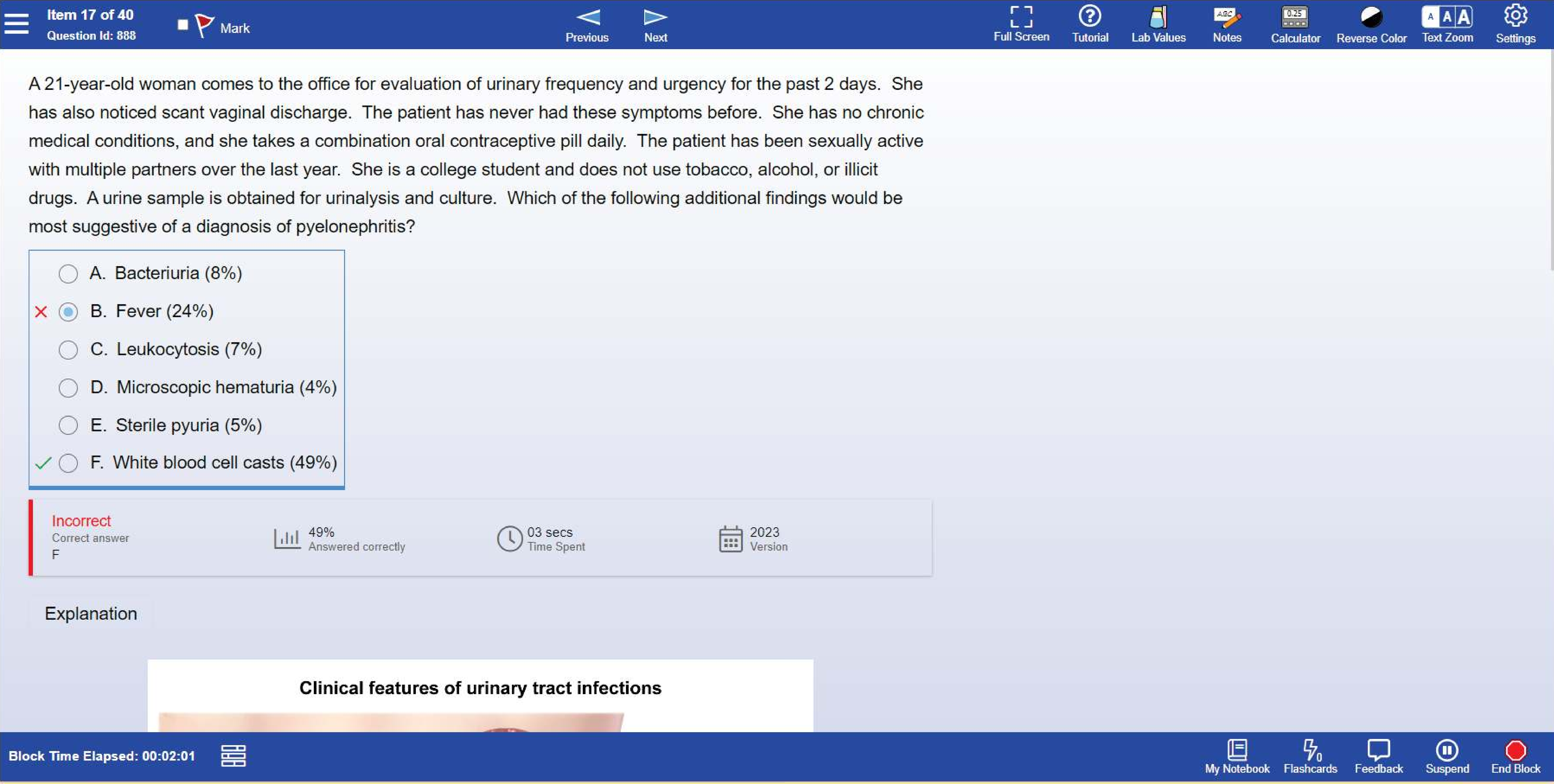
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- ○ A. Bacteriuria (8%)
- ✗ ● B. Fever (24%)
- ○ C. Leukocytosis (7%)
- ○ D. Microscopic hematuria (4%)
- ○ E. Sterile pyuria (5%)
- ✓ ○ F. White blood cell casts (49%)

Incorrect
Correct answer
F

49%
Answered correctly

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Explanation

Clinical features of urinary tract infections

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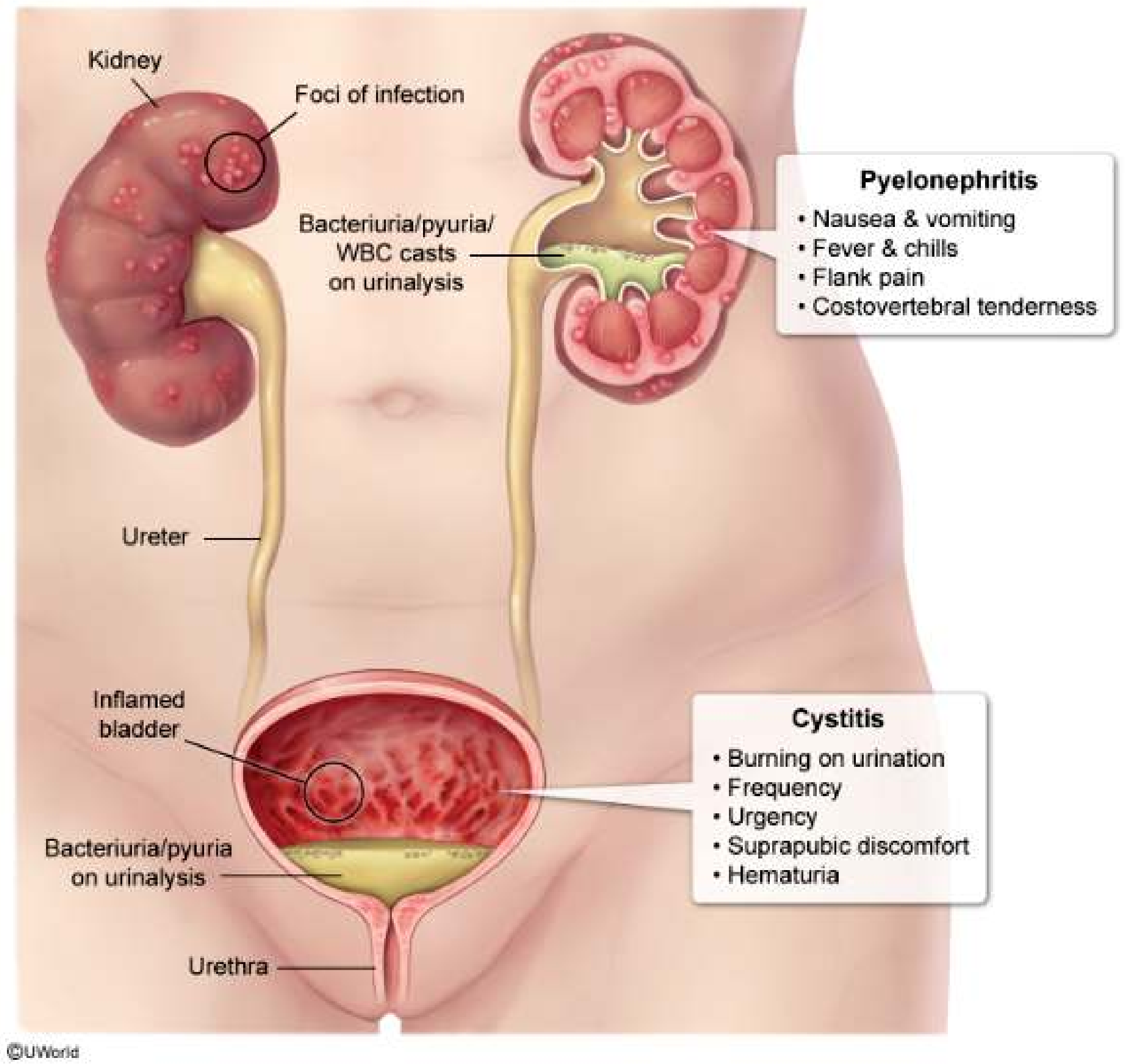
Clinical features of urinary tract infections


Kidney
Foci of infection
Bacteriuria/pyuria/
WBC casts
on urinalysis
Ureter
Inflamed
bladder
Bacteriuria/pyuria
on urinalysis
Urethra

Pyelonephritis

- Nausea & vomiting
- Fever & chills
- Flank pain
- Costovertebral tenderness

Cystitis

- Burning on urination
- Frequency
- Urgency
- Suprapubic discomfort
- Hematuria

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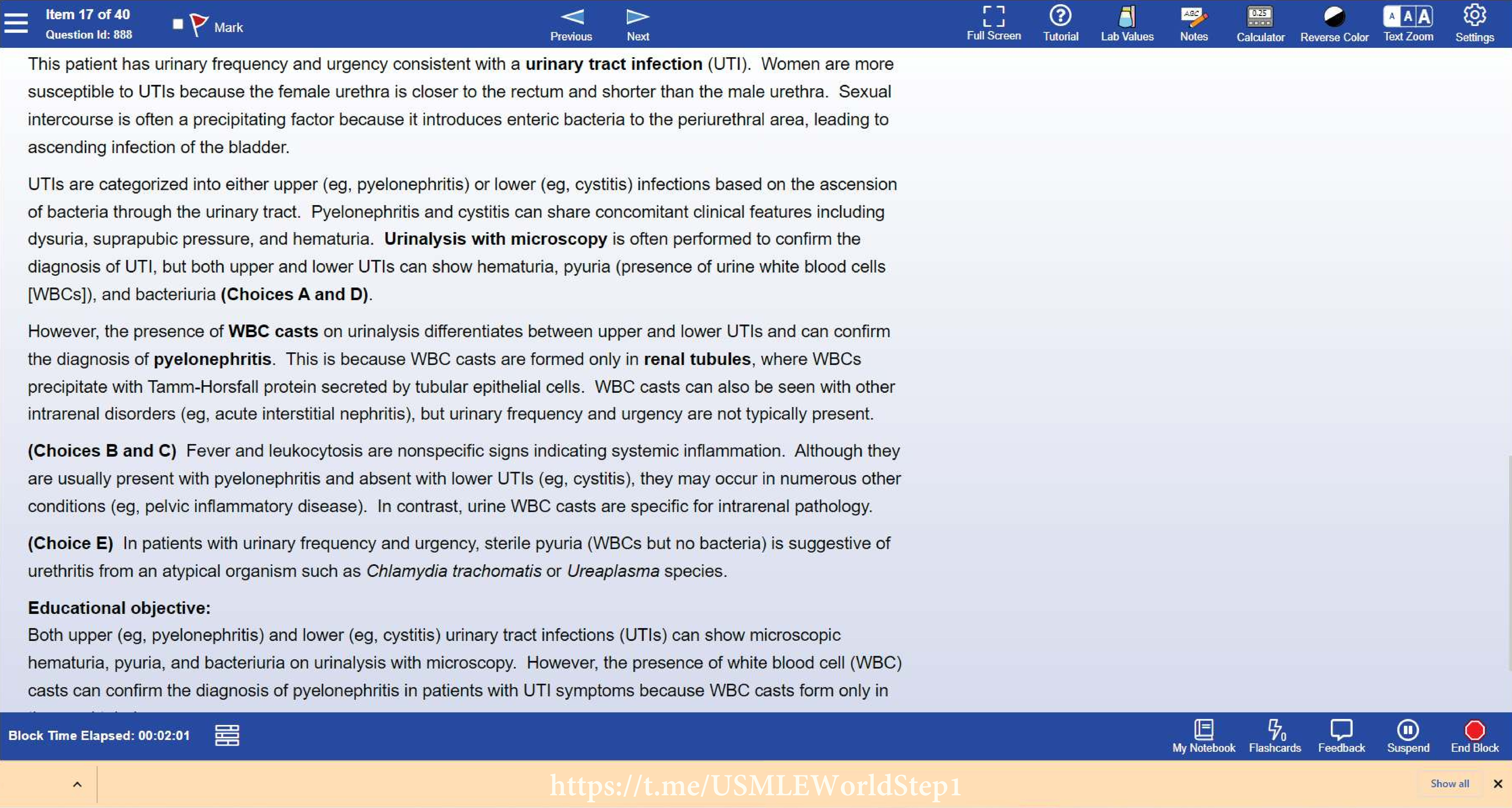


This patient has urinary frequency and urgency consistent with a **urinary tract infection** (UTI). Women are more susceptible to UTIs because the female urethra is closer to the rectum and shorter than the male urethra. Sexual intercourse is often a precipitating factor because it introduces enteric bacteria to the periurethral area, leading to ascending infection of the bladder.

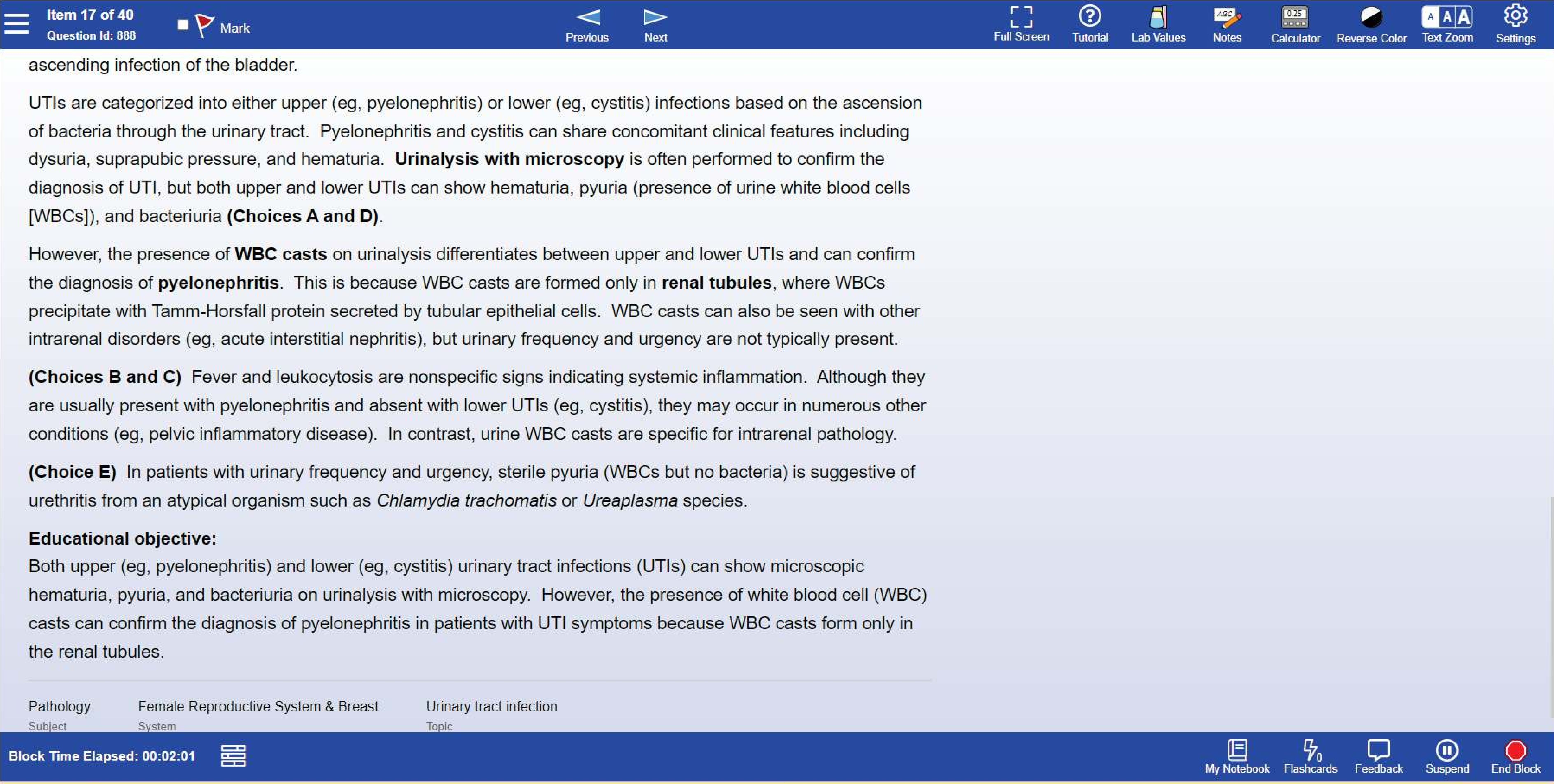
UTIs are categorized into either upper (eg, pyelonephritis) or lower (eg, cystitis) infections based on the ascension of bacteria through the urinary tract. Pyelonephritis and cystitis can share concomitant clinical features including dysuria, suprapubic pressure, and hematuria. **Urinalysis with microscopy** is often performed to confirm the diagnosis of UTI, but both upper and lower UTIs can show hematuria, pyuria (presence of urine white blood cells [WBCs]), and bacteriuria **(Choices A and D)**.

However, the presence of **WBC casts** on urinalysis differentiates between upper and lower UTIs and can confirm the diagnosis of **pyelonephritis**. This is because WBC casts are formed only in **renal tubules**, where WBCs precipitate with Tamm-Horsfall protein secreted by tubular epithelial cells. WBC casts can also be seen with other intrarenal disorders (eg, acute interstitial nephritis), but urinary frequency and urgency are not typically present.

(Choices B and C) Fever and leukocytosis are nonspecific signs indicating systemic inflammation. Although they are usually present with pyelonephritis and absent with lower UTIs (eg, cystitis), they may occur in numerous other conditions (eg, pelvic inflammatory disease). In contrast, urine WBC casts are specific for intrarenal pathology.

(Choice E) In patients with urinary frequency and urgency, sterile pyuria (WBCs but no bacteria) is suggestive of urethritis from an atypical organism such as *Chlamydia trachomatis* or *Ureaplasma* species.

Educational objective:
Both upper (eg, pyelonephritis) and lower (eg, cystitis) urinary tract infections (UTIs) can show microscopic hematuria, pyuria, and bacteriuria on urinalysis with microscopy. However, the presence of white blood cell (WBC) casts can confirm the diagnosis of pyelonephritis in patients with UTI symptoms because WBC casts form only in



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ascending infection of the bladder.

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Educational objective:

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Pathology	Female Reproductive System & Breast	Urinary tract infection
Subject	System	Topic

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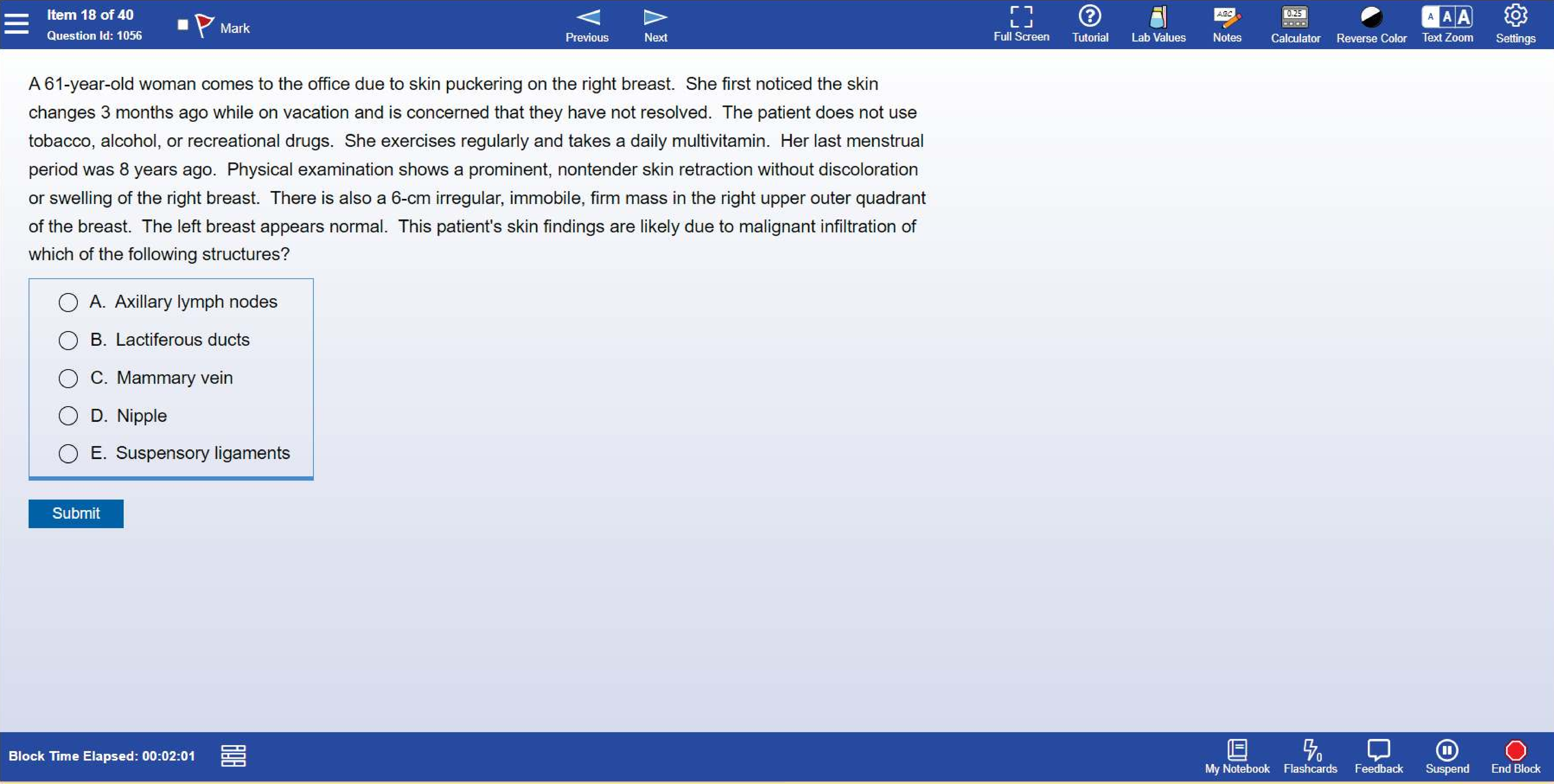
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Question Id: 1056

A 61-year-old woman comes to the office due to skin puckering on the right breast. She first noticed the skin changes 3 months ago while on vacation and is concerned that they have not resolved. The patient does not use tobacco, alcohol, or recreational drugs. She exercises regularly and takes a daily multivitamin. Her last menstrual period was 8 years ago. Physical examination shows a prominent, nontender skin retraction without discoloration or swelling of the right breast. There is also a 6-cm irregular, immobile, firm mass in the right upper outer quadrant of the breast. The left breast appears normal. This patient's skin findings are likely due to malignant infiltration of which of the following structures?

- ○ A. Axillary lymph nodes
- ○ B. Lactiferous ducts
- ○ C. Mammary vein
- ○ D. Nipple
- ○ E. Suspensory ligaments

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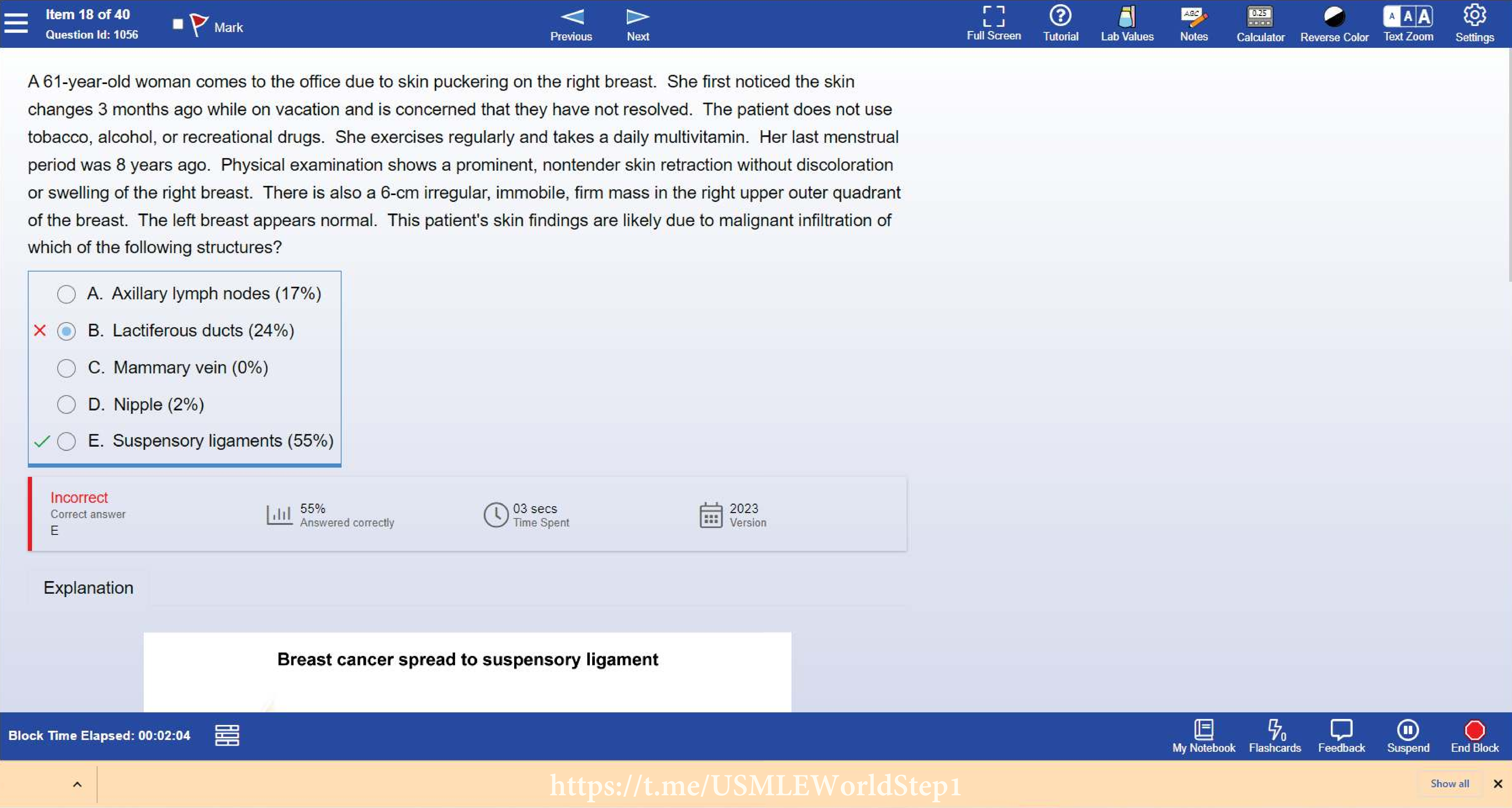
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○ A. Axillary lymph nodes (17%)

✗ ● B. Lactiferous ducts (24%)

○ C. Mammary vein (0%)

○ D. Nipple (2%)

✓ ○ E. Suspensory ligaments (55%)

Incorrect
Correct answer
E

55%
Answered correctly

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Explanation

Breast cancer spread to suspensory ligament

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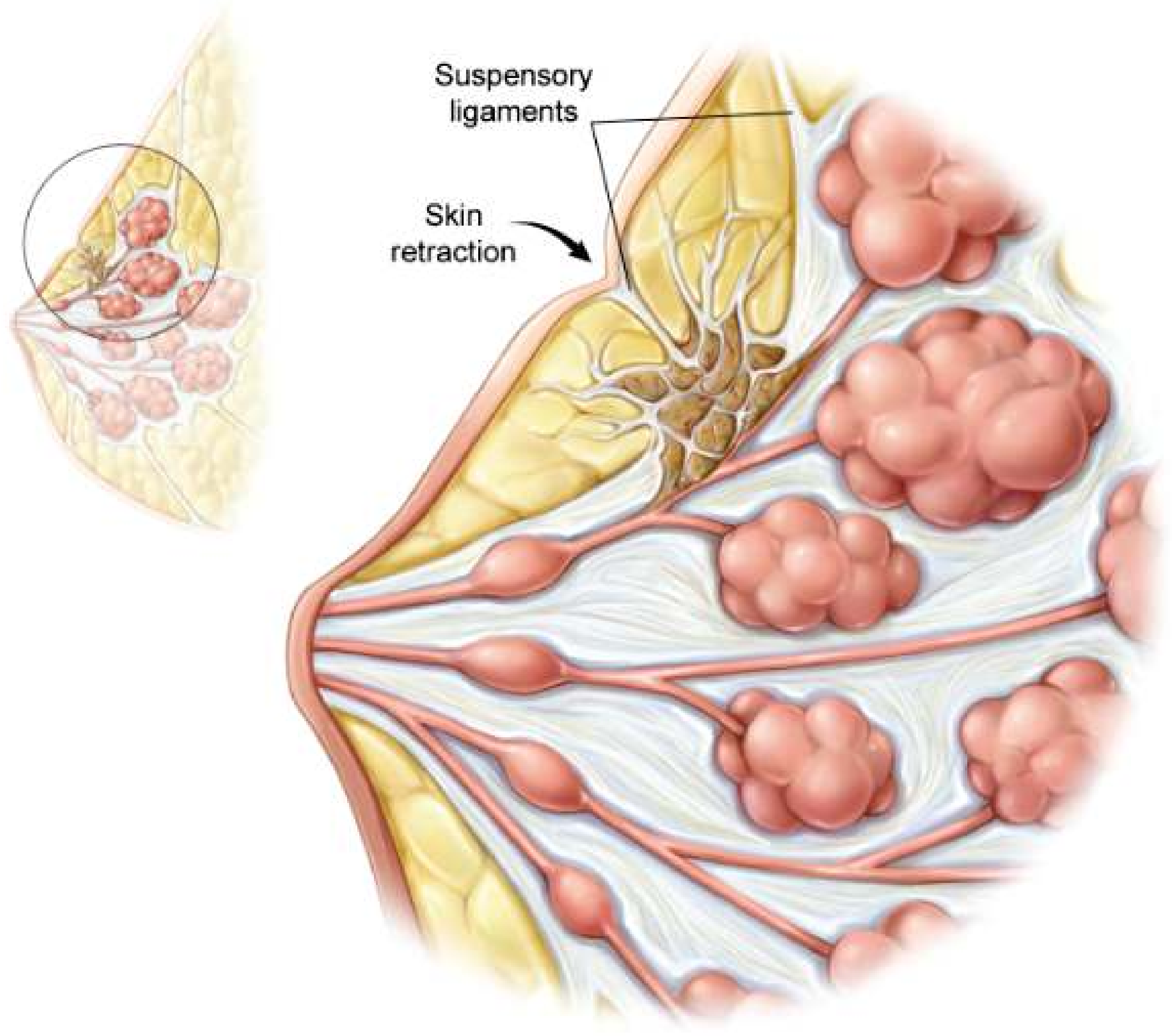
Breast cancer spread to suspensory ligament


Suspensory ligaments
Skin retraction

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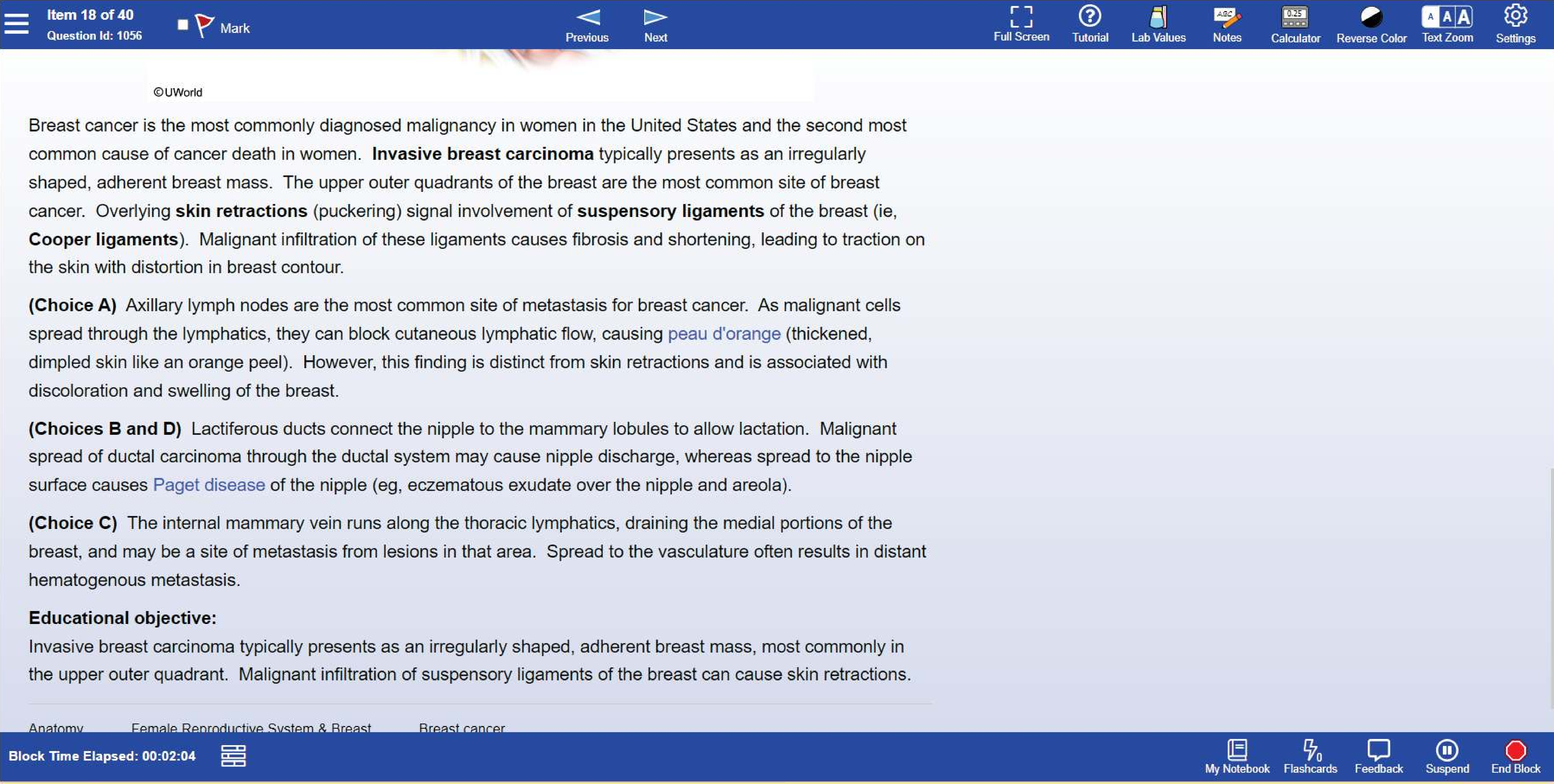
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Breast cancer is the most commonly diagnosed malignancy in women in the United States and the second most common cause of cancer death in women. **Invasive breast carcinoma** typically presents as an irregularly shaped, adherent breast mass. The upper outer quadrants of the breast are the most common site of breast cancer. Overlying **skin retractions** (puckering) signal involvement of **suspensory ligaments** of the breast (ie, **Cooper ligaments**). Malignant infiltration of these ligaments causes fibrosis and shortening, leading to traction on the skin with distortion in breast contour.

(Choice A) Axillary lymph nodes are the most common site of metastasis for breast cancer. As malignant cells spread through the lymphatics, they can block cutaneous lymphatic flow, causing peau d'orange (thickened, dimpled skin like an orange peel). However, this finding is distinct from skin retractions and is associated with discoloration and swelling of the breast.

(Choices B and D) Lactiferous ducts connect the nipple to the mammary lobules to allow lactation. Malignant spread of ductal carcinoma through the ductal system may cause nipple discharge, whereas spread to the nipple surface causes Paget disease of the nipple (eg, eczematous exudate over the nipple and areola).

(Choice C) The internal mammary vein runs along the thoracic lymphatics, draining the medial portions of the breast, and may be a site of metastasis from lesions in that area. Spread to the vasculature often results in distant hematogenous metastasis.

Educational objective:

Invasive breast carcinoma typically presents as an irregularly shaped, adherent breast mass, most commonly in the upper outer quadrant. Malignant infiltration of suspensory ligaments of the breast can cause skin retractions.

Anatomy Female Reproductive System & Breast Breast cancer

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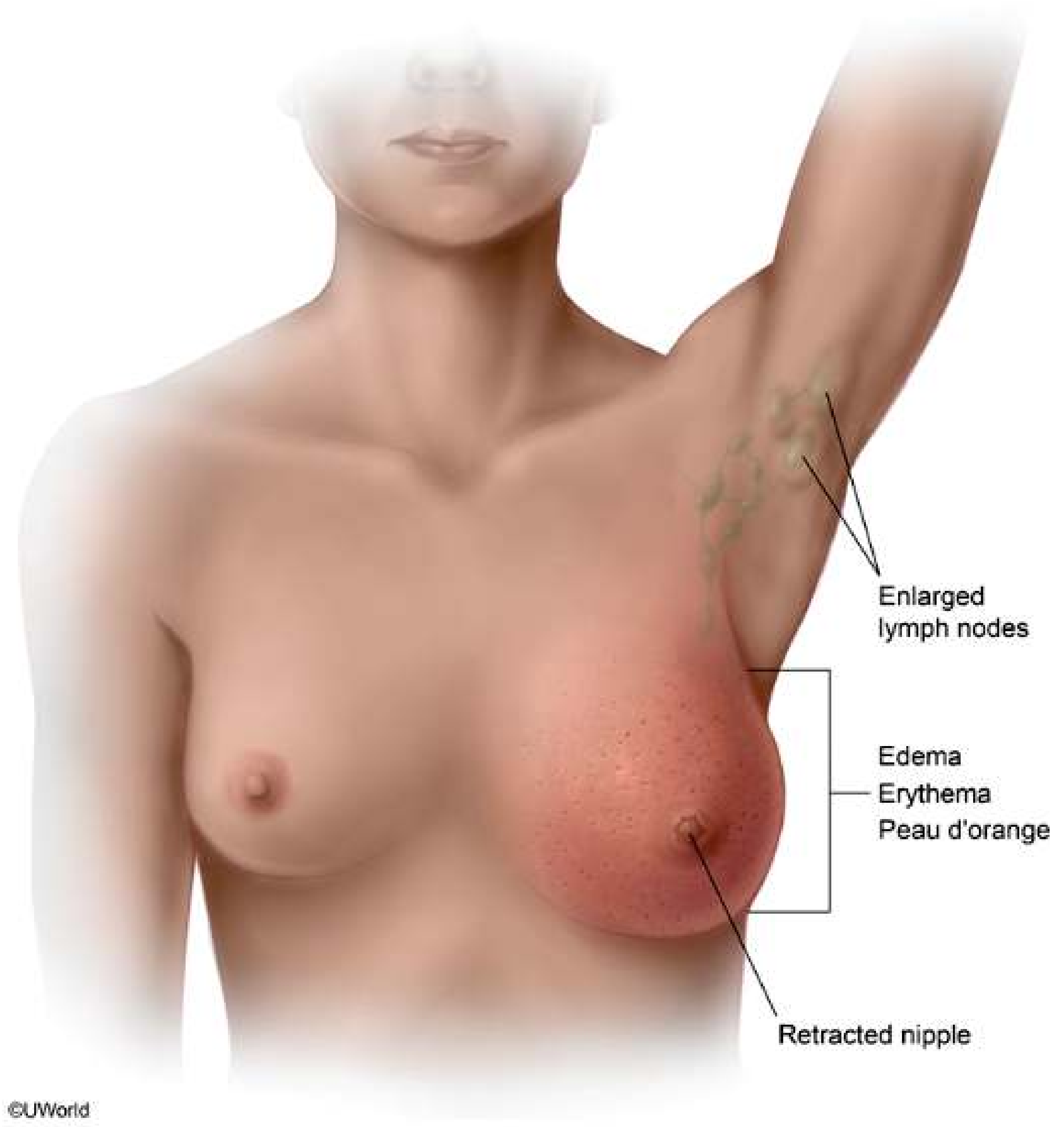
Inflammatory breast cancer


Enlarged
lymph nodes
Edema
Erythema
Peau d'orange
Retracted nipple
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Anatomy | Female Reproductive System & Breast | Breast cancer

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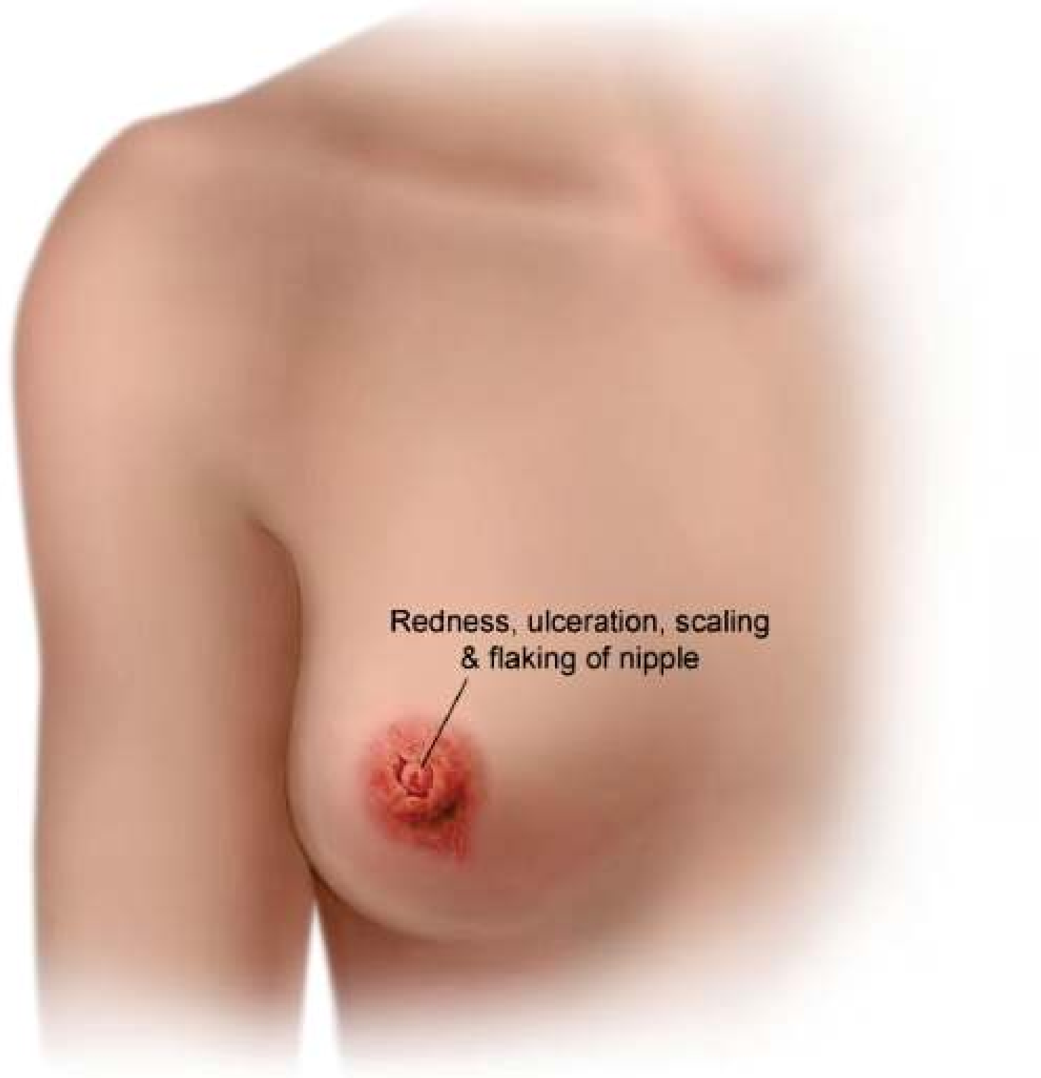
Mammary Paget disease



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Anatomy Female Reproductive System & Breast Breast cancer

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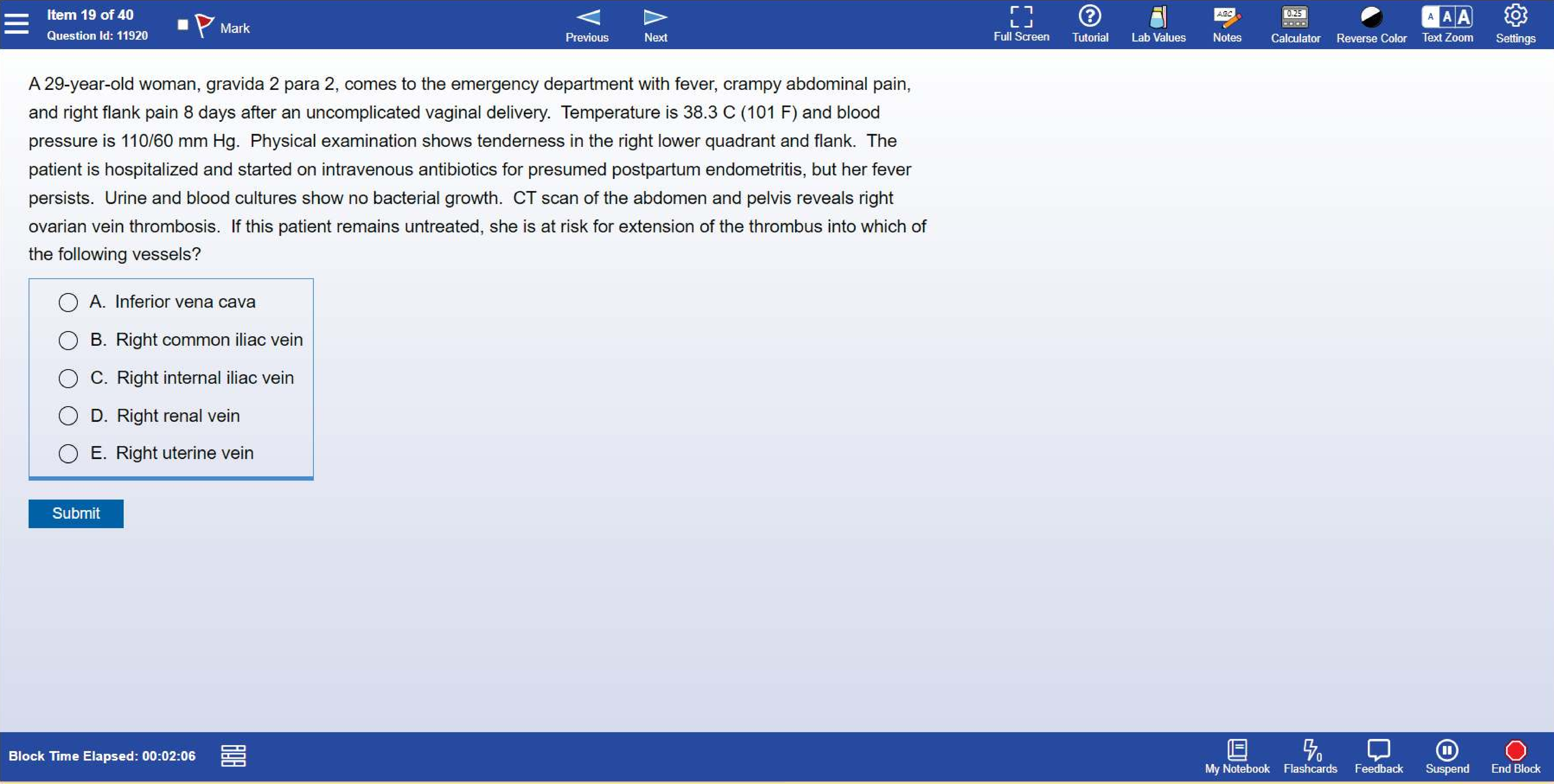
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A 29-year-old woman, gravida 2 para 2, comes to the emergency department with fever, crampy abdominal pain, and right flank pain 8 days after an uncomplicated vaginal delivery. Temperature is 38.3 C (101 F) and blood pressure is 110/60 mm Hg. Physical examination shows tenderness in the right lower quadrant and flank. The patient is hospitalized and started on intravenous antibiotics for presumed postpartum endometritis, but her fever persists. Urine and blood cultures show no bacterial growth. CT scan of the abdomen and pelvis reveals right ovarian vein thrombosis. If this patient remains untreated, she is at risk for extension of the thrombus into which of the following vessels?

○ A. Inferior vena cava
○ B. Right common iliac vein
○ C. Right internal iliac vein
○ D. Right renal vein
○ E. Right uterine vein

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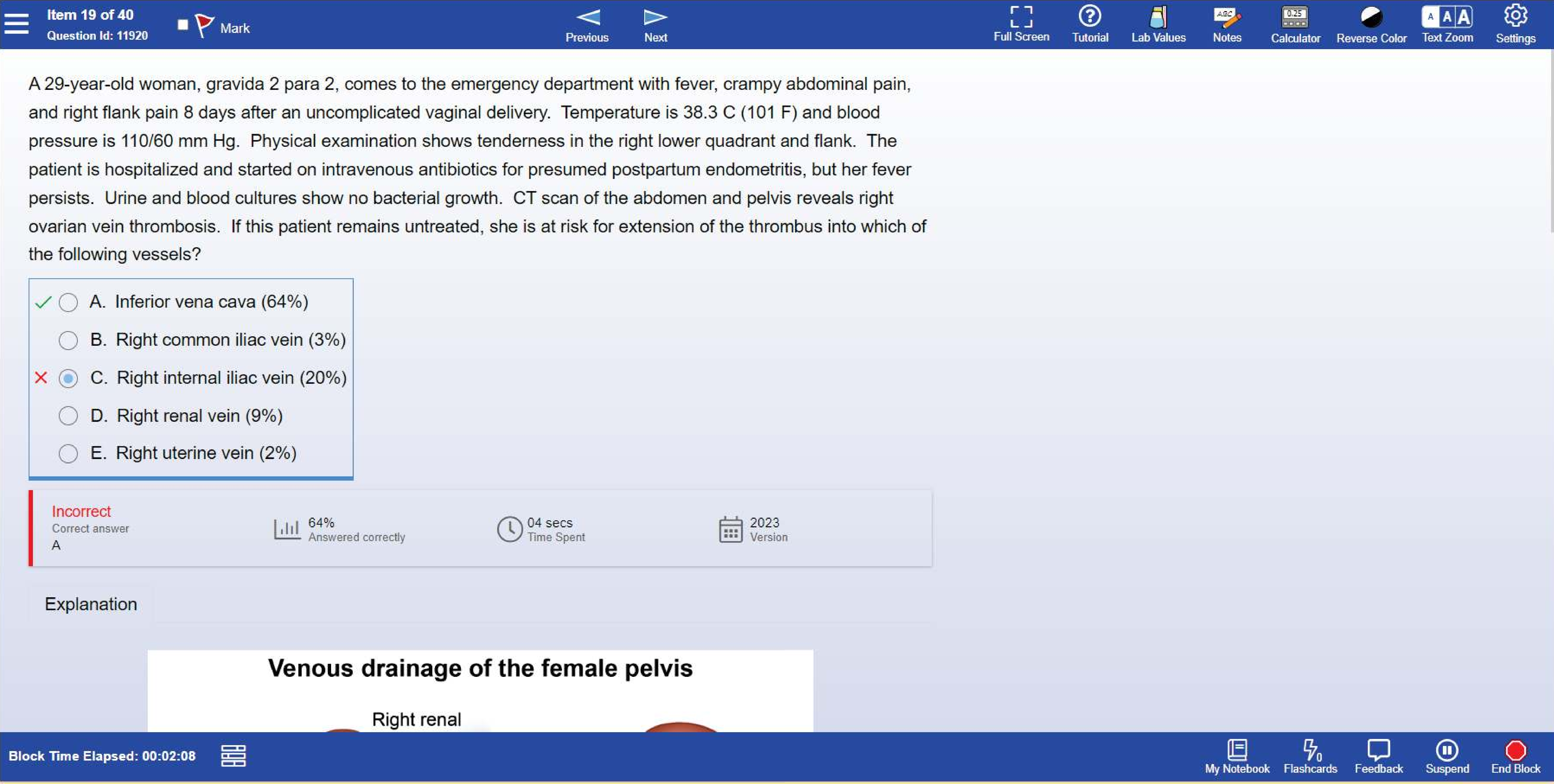
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✓ ○ A. Inferior vena cava (64%)

○ B. Right common iliac vein (3%)

✗ ● C. Right internal iliac vein (20%)

○ D. Right renal vein (9%)

○ E. Right uterine vein (2%)

Incorrect
Correct answer
A

64%
Answered correctly

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Explanation

Venous drainage of the female pelvis

Right renal
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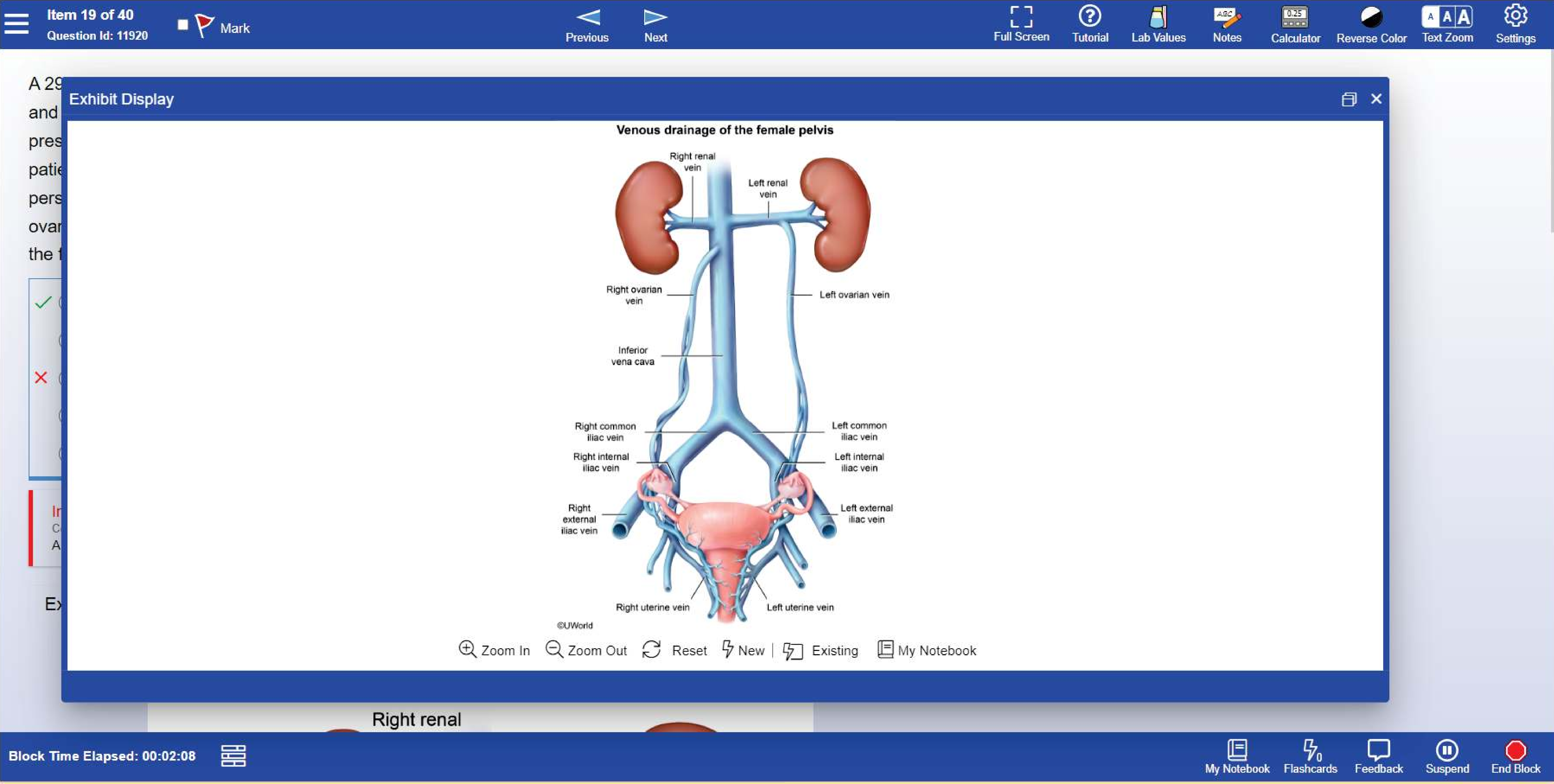
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Exhibit Display
Venous drainage of the female pelvis
Right renal vein
Left renal vein
Right ovarian vein
Left ovarian vein
Inferior vena cava
Right common iliac vein
Left common iliac vein
Right internal iliac vein
Left internal iliac vein
Right external iliac vein
Left external iliac vein
Right uterine vein
Left uterine vein
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Right renal
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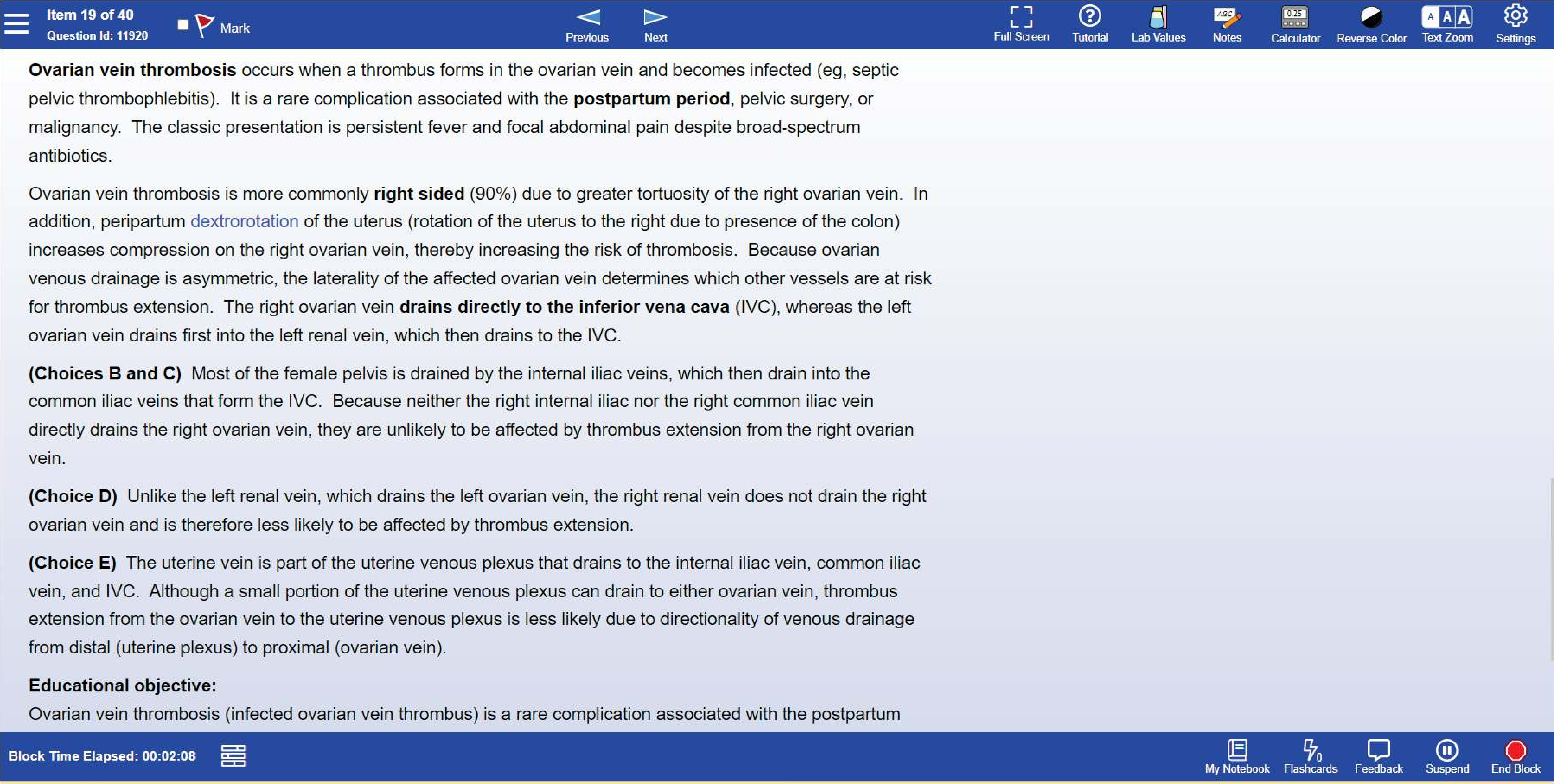


Ovarian vein thrombosis occurs when a thrombus forms in the ovarian vein and becomes infected (eg, septic pelvic thrombophlebitis). It is a rare complication associated with the **postpartum period**, pelvic surgery, or malignancy. The classic presentation is persistent fever and focal abdominal pain despite broad-spectrum antibiotics.

Ovarian vein thrombosis is more commonly **right sided** (90%) due to greater tortuosity of the right ovarian vein. In addition, peripartum dextrorotation of the uterus (rotation of the uterus to the right due to presence of the colon) increases compression on the right ovarian vein, thereby increasing the risk of thrombosis. Because ovarian venous drainage is asymmetric, the laterality of the affected ovarian vein determines which other vessels are at risk for thrombus extension. The right ovarian vein **drains directly to the inferior vena cava** (IVC), whereas the left ovarian vein drains first into the left renal vein, which then drains to the IVC.

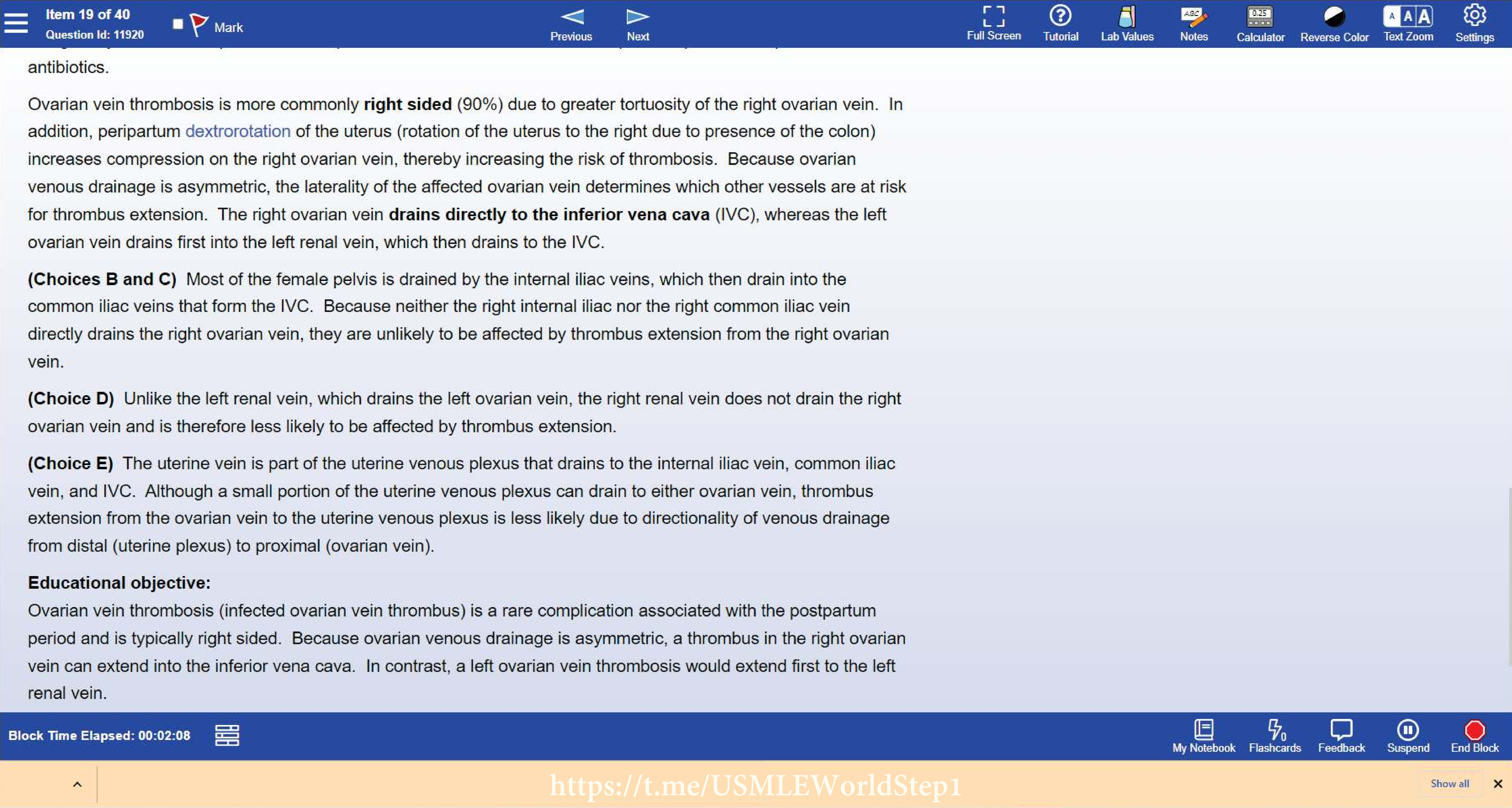
(Choices B and C) Most of the female pelvis is drained by the internal iliac veins, which then drain into the common iliac veins that form the IVC. Because neither the right internal iliac nor the right common iliac vein directly drains the right ovarian vein, they are unlikely to be affected by thrombus extension from the right ovarian vein.

(Choice D) Unlike the left renal vein, which drains the left ovarian vein, the right renal vein does not drain the right ovarian vein and is therefore less likely to be affected by thrombus extension.

(Choice E) The uterine vein is part of the uterine venous plexus that drains to the internal iliac vein, common iliac vein, and IVC. Although a small portion of the uterine venous plexus can drain to either ovarian vein, thrombus extension from the ovarian vein to the uterine venous plexus is less likely due to directionality of venous drainage from distal (uterine plexus) to proximal (ovarian vein).

Educational objective:

Ovarian vein thrombosis (infected ovarian vein thrombus) is a rare complication associated with the postpartum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antibiotics.

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Educational objective:

Ovarian vein thrombosis (infected ovarian vein thrombus) is a rare complication associated with the postpartum period and is typically right sided. Because ovarian venous drainage is asymmetric, a thrombus in the right ovarian vein can extend into the inferior vena cava. In contrast, a left ovarian vein thrombosis would extend first to the left renal vein.

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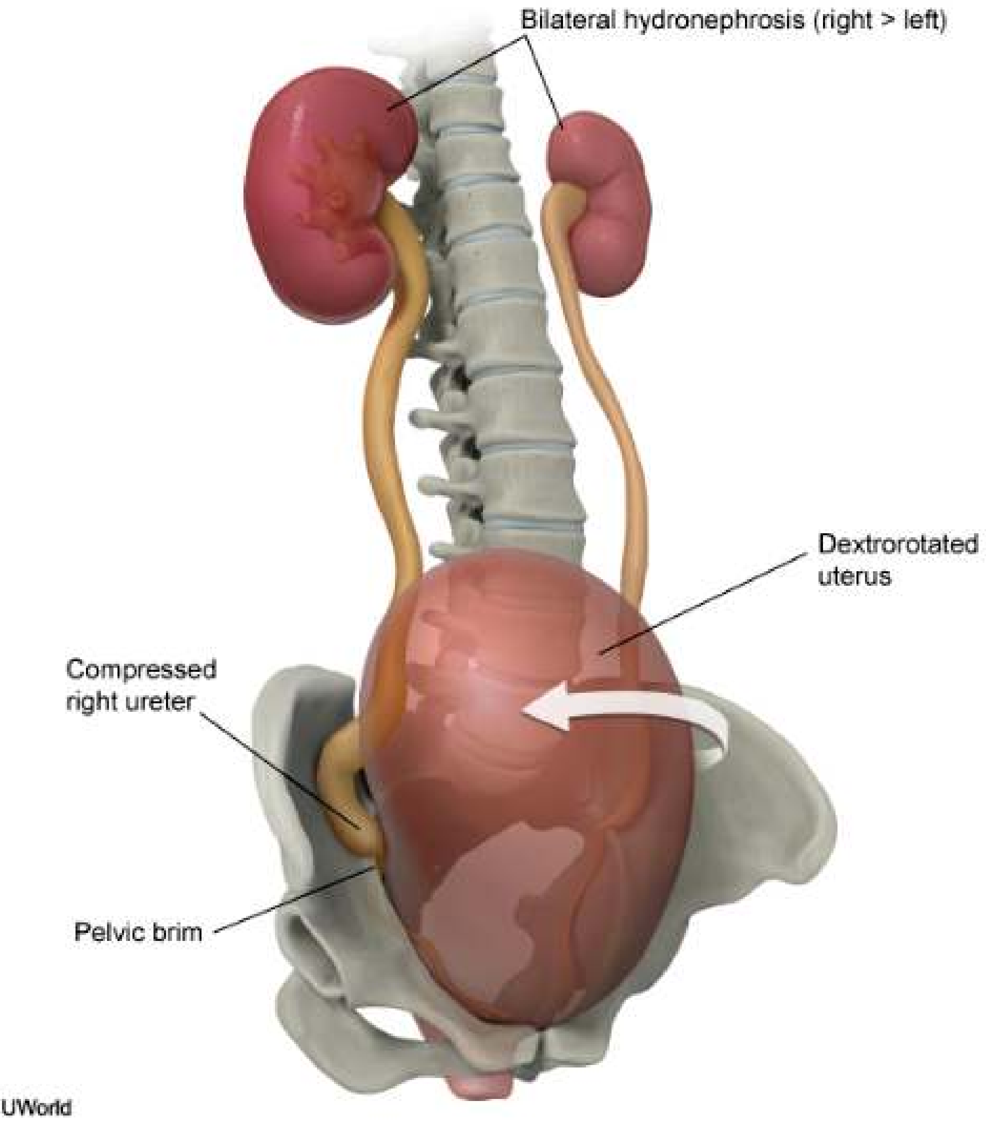
Physiologic hydronephrosis of pregnancy


Bilateral hydronephrosis (right > left)
Dextrorotated uterus
Compressed right ureter
Pelvic brim
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extension from the ovarian vein to the uterine venous plexus is less likely due to directionality of venous drainage from distal (uterine plexus) to proximal (ovarian vein).

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A 40-year-old woman, gravida 5, para 0, aborta 4, at 12 weeks gestation comes to the emergency department due to vaginal bleeding, midline pelvic pain, and severe nausea and vomiting. She has a history of 4 prior first trimester losses. Pelvic examination shows a 16-week-sized uterus. Speculum examination reveals dark red blood in the vagina. A β-hCG level is >100,000 mIU/mL, and an ultrasound shows no fetus and a uterine cavity filled with multiple small cysts. The patient undergoes dilation and curettage in the operating room, and a friable mass of tissue consisting of many thin-walled cysts is evacuated from her uterus. Examination of the tissue would most likely show which of the following karyotypes?

- ○ A. 46,XX
- ○ B. 46,XY
- ○ C. 47,XXX
- ○ D. 47,XXY
- ○ E. 69,XXX
- ○ F. 69,XXY

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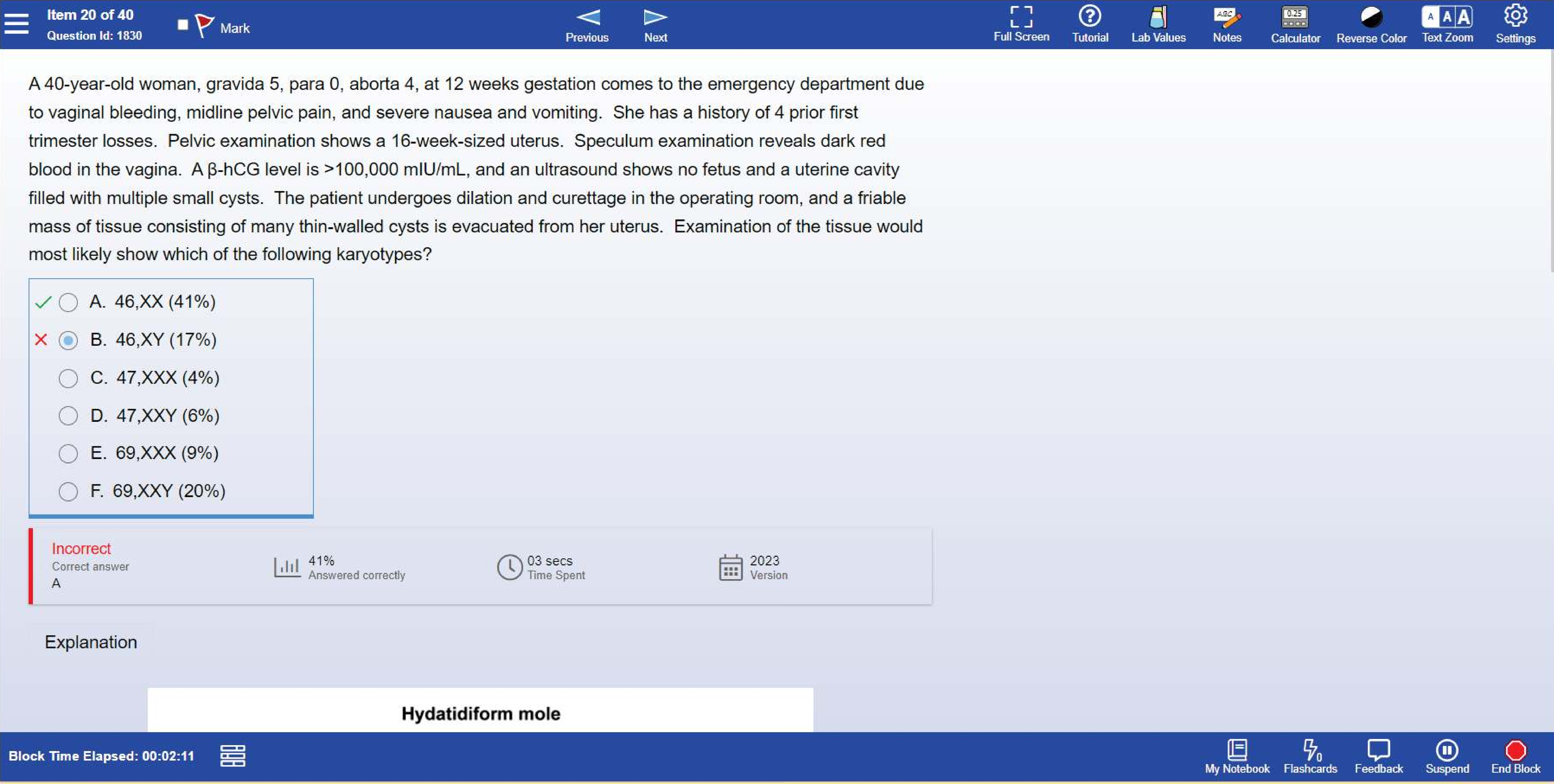
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- ✓ ○ A. 46,XX (41%)
- ✗ ● B. 46,XY (17%)
- ○ C. 47,XXX (4%)
- ○ D. 47,XXY (6%)
- ○ E. 69,XXX (9%)
- ○ F. 69,XXY (20%)

Incorrect
Correct answer
A

41%
Answered correctly

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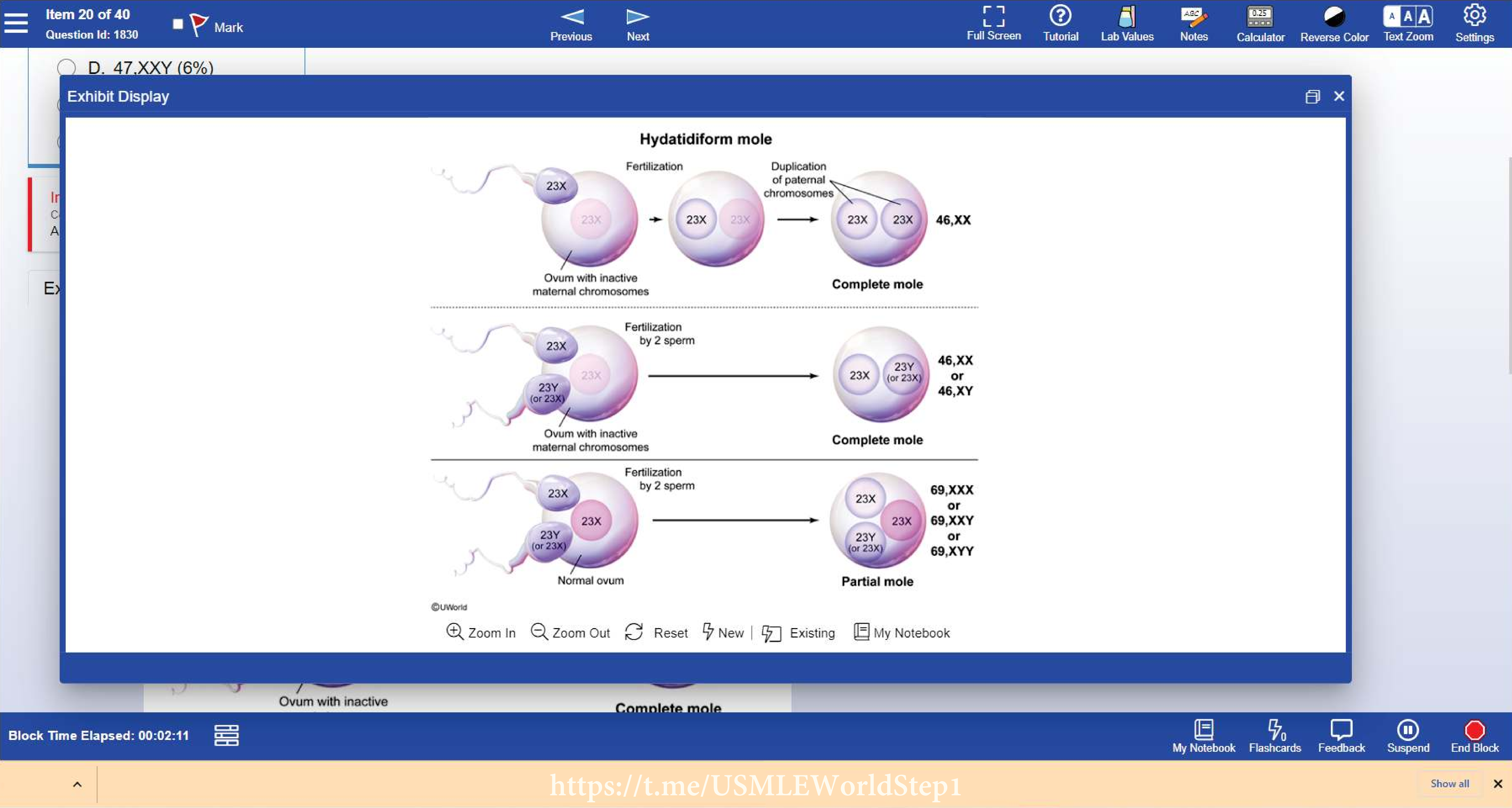
Explanation

Hydatidiform mole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○ D. 47,XXY (6%)

Exhibit Display

Hydatidiform mole

Fertilization
23X
23X
Ovum with inactive maternal chromosomes
23X
23X
Duplication of paternal chromosomes
23X
23X
46,XX
Complete mole
Fertilization by 2 sperm
23X
23X
23Y (or 23X)
Ovum with inactive maternal chromosomes
23X
23Y (or 23X)
46,XX or 46,XY
Complete mole
Fertilization by 2 sperm
23X
23X
23Y (or 23X)
Normal ovum
23X
23X
23Y (or 23X)
69,XXX or 69,XXY or 69,XYY
Partial mole
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Ovum with inactive
Complete mole
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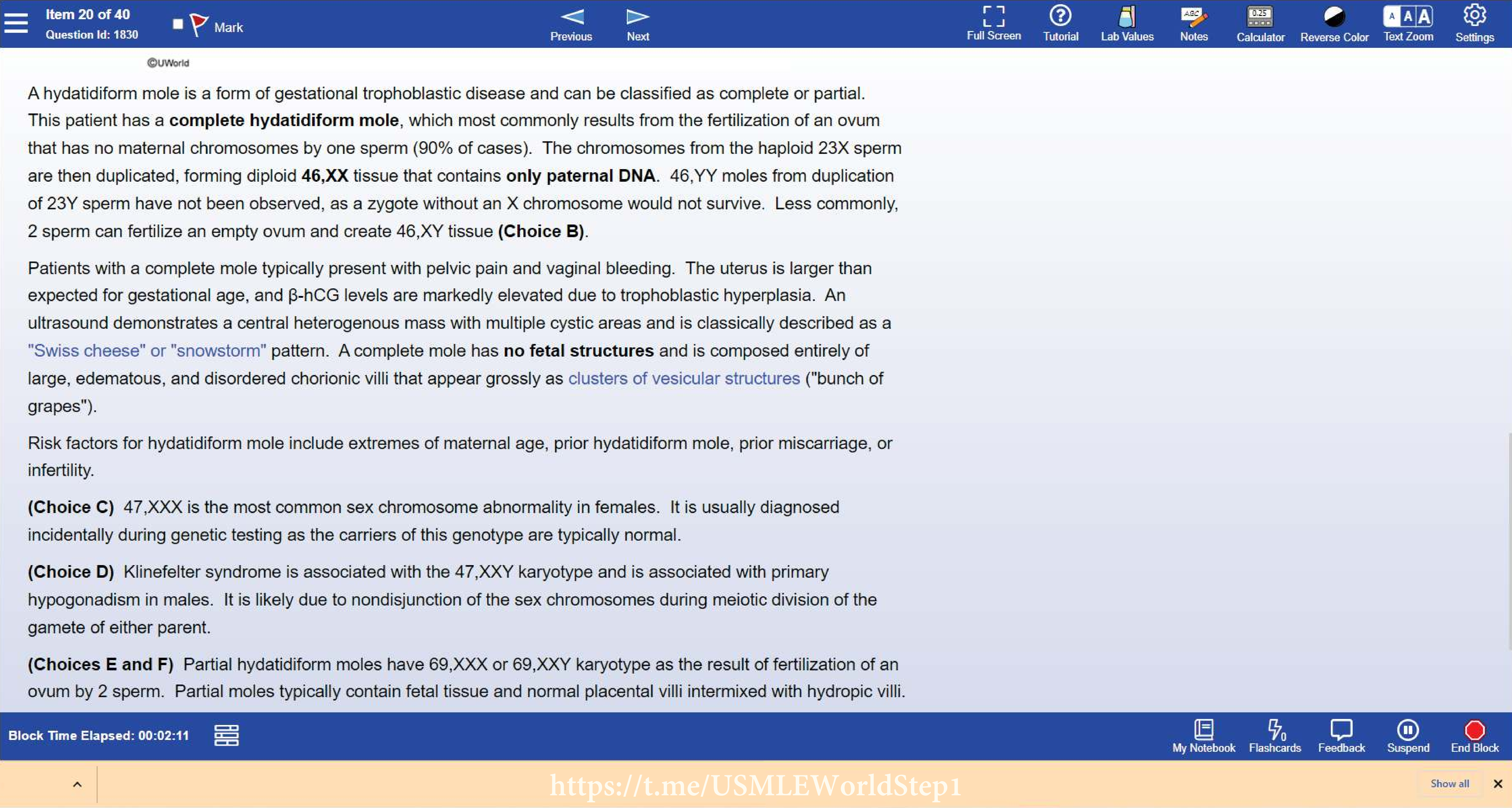
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A hydatidiform mole is a form of gestational trophoblastic disease and can be classified as complete or partial. This patient has a **complete hydatidiform mole**, which most commonly results from the fertilization of an ovum that has no maternal chromosomes by one sperm (90% of cases). The chromosomes from the haploid 23X sperm are then duplicated, forming diploid **46,XX** tissue that contains **only paternal DNA**. 46,YY moles from duplication of 23Y sperm have not been observed, as a zygote without an X chromosome would not survive. Less commonly, 2 sperm can fertilize an empty ovum and create 46,XY tissue **(Choice B)**.

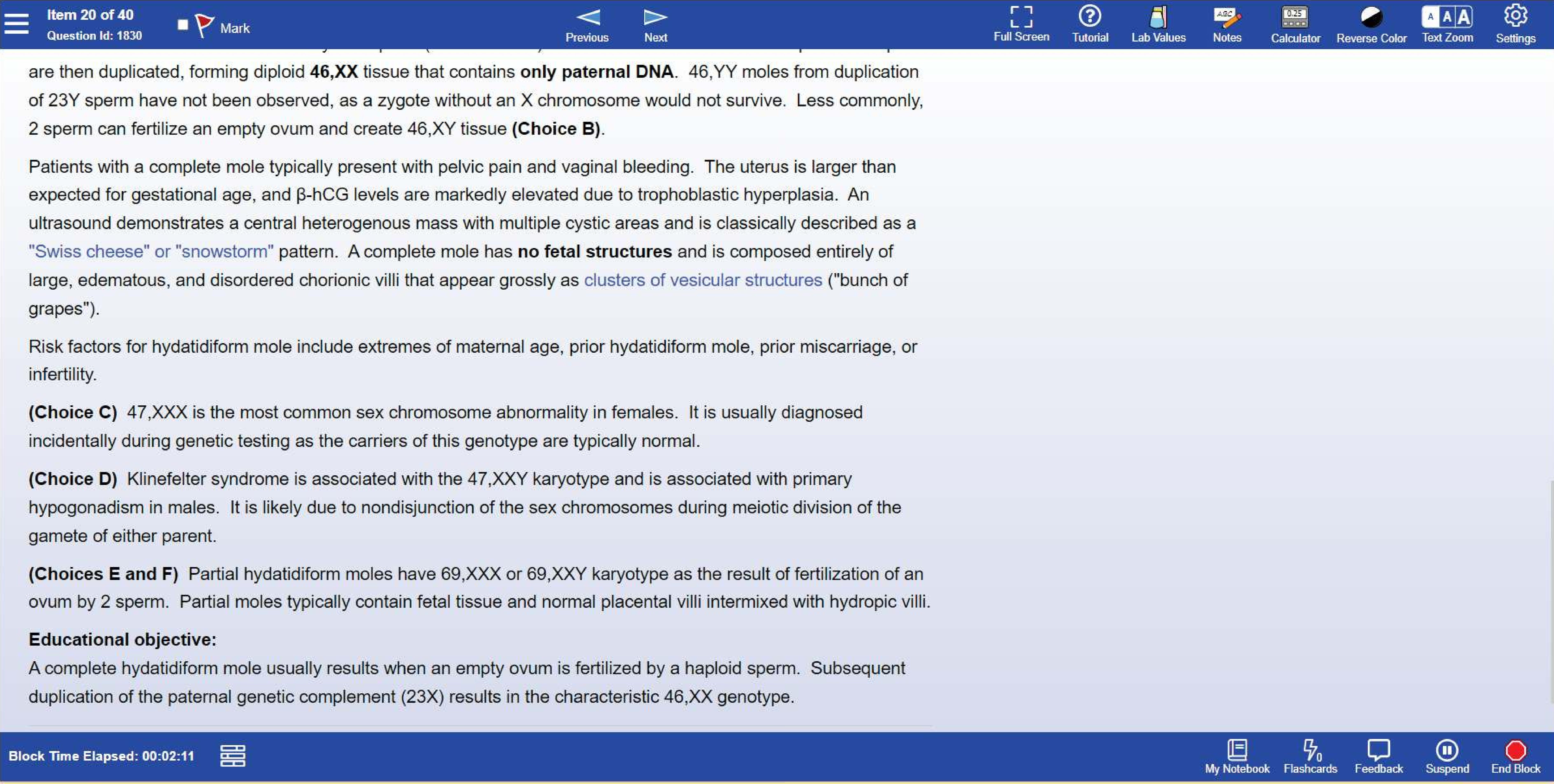
Patients with a complete mole typically present with pelvic pain and vaginal bleeding. The uterus is larger than expected for gestational age, and β-hCG levels are markedly elevated due to trophoblastic hyperplasia. An ultrasound demonstrates a central heterogenous mass with multiple cystic areas and is classically described as a "Swiss cheese" or "snowstorm" pattern. A complete mole has **no fetal structures** and is composed entirely of large, edematous, and disordered chorionic villi that appear grossly as clusters of vesicular structures ("bunch of grapes").

Risk factors for hydatidiform mole include extremes of maternal age, prior hydatidiform mole, prior miscarriage, or infertility.

(Choice C) 47,XXX is the most common sex chromosome abnormality in females. It is usually diagnosed incidentally during genetic testing as the carriers of this genotype are typically normal.

(Choice D) Klinefelter syndrome is associated with the 47,XXY karyotype and is associated with primary hypogonadism in males. It is likely due to nondisjunction of the sex chromosomes during meiotic division of the gamete of either parent.

(Choices E and F) Partial hydatidiform moles have 69,XXX or 69,XXY karyotype as the result of fertilization of an ovum by 2 sperm. Partial moles typically contain fetal tissue and normal placental villi intermixed with hydropic villi.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Educational objective:

A complete hydatidiform mole usually results when an empty ovum is fertilized by a haploid sperm. Subsequent duplication of the paternal genetic complement (23X) results in the characteristic 46,XX genotype.

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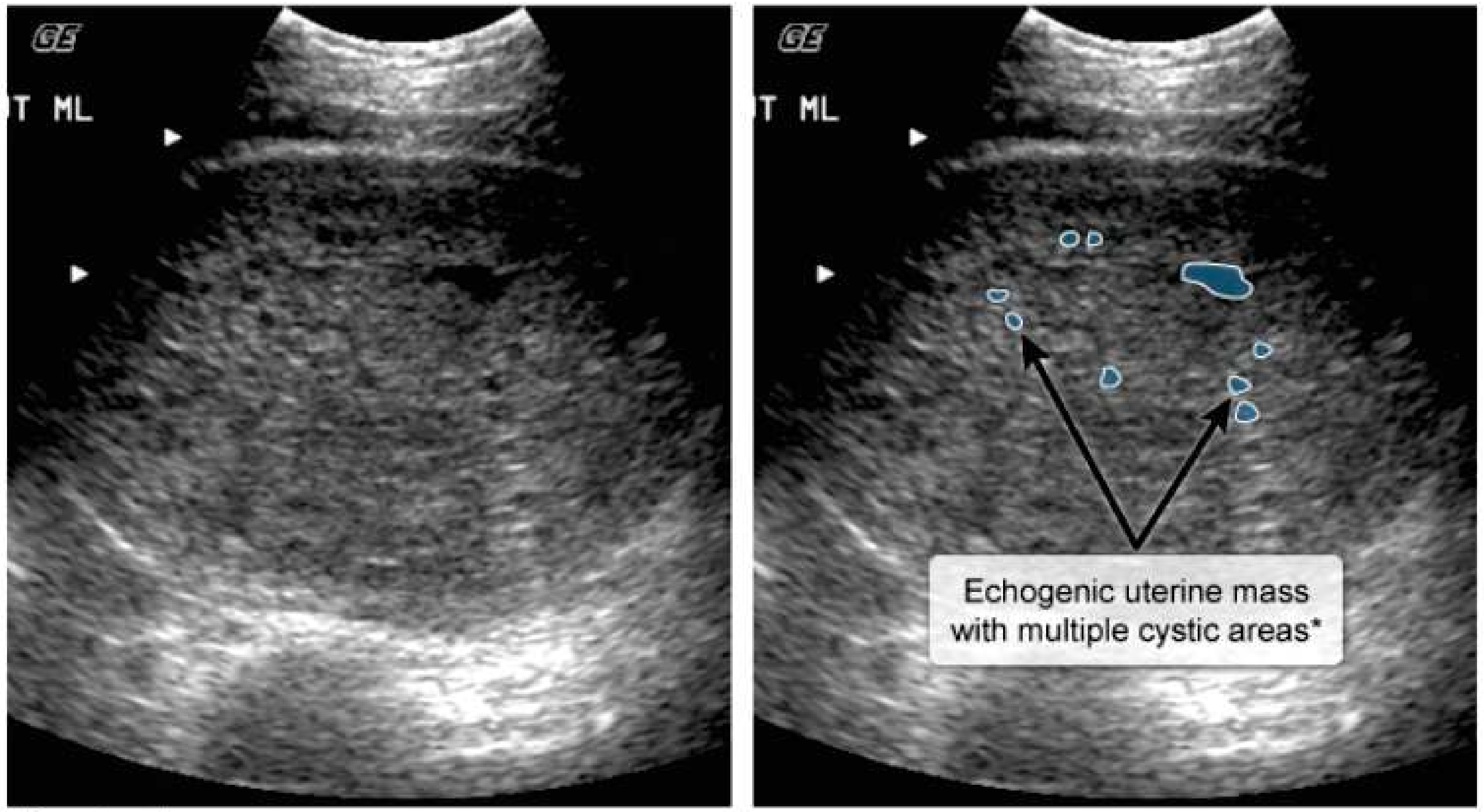
Complete hydatidiform mole


GE
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GE
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Echogenic uterine mass with multiple cystic areas*

*"Snowstorm" appearance

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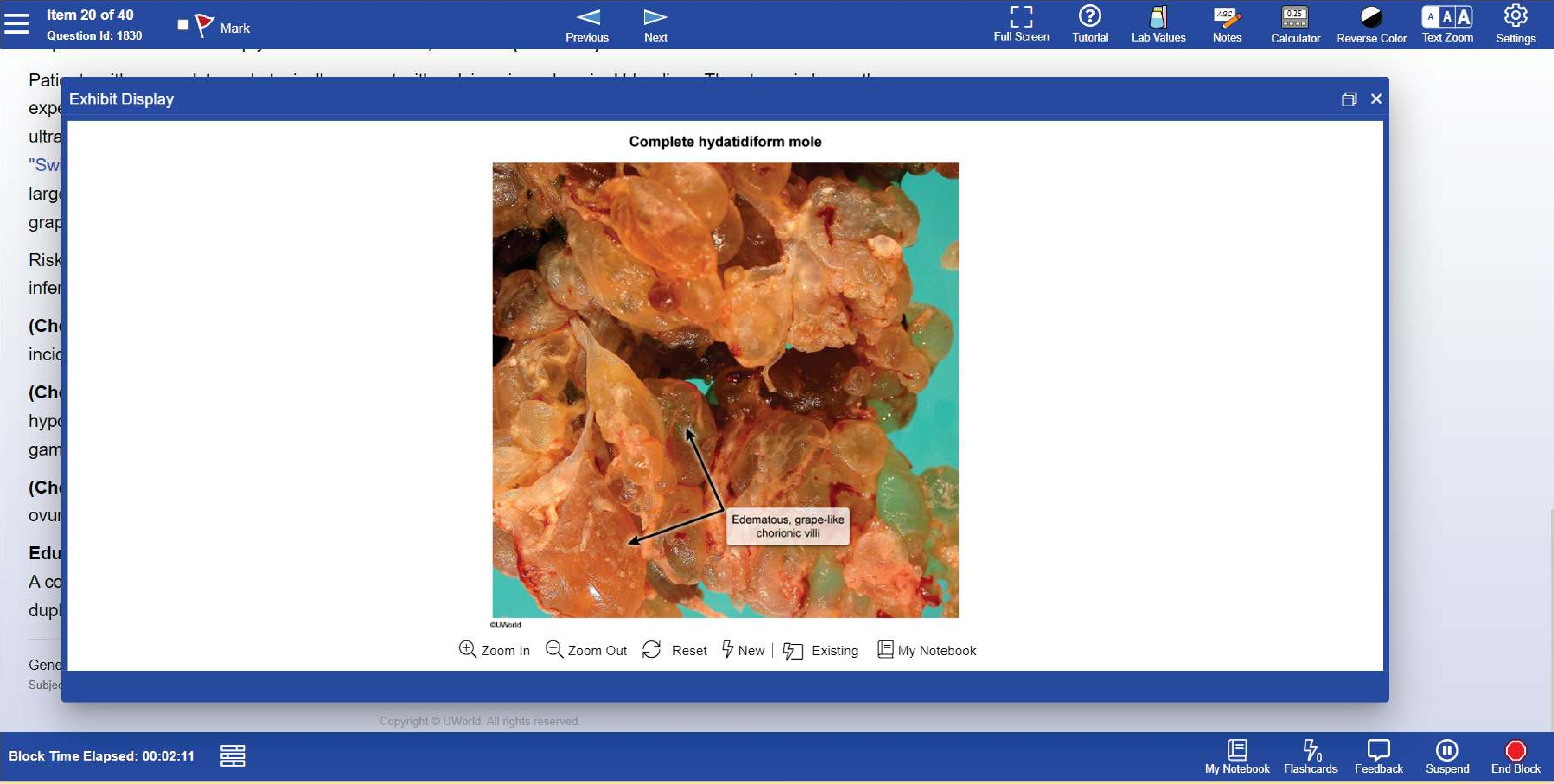
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Complete hydatidiform mole

Edematous, grape-like chorionic villi

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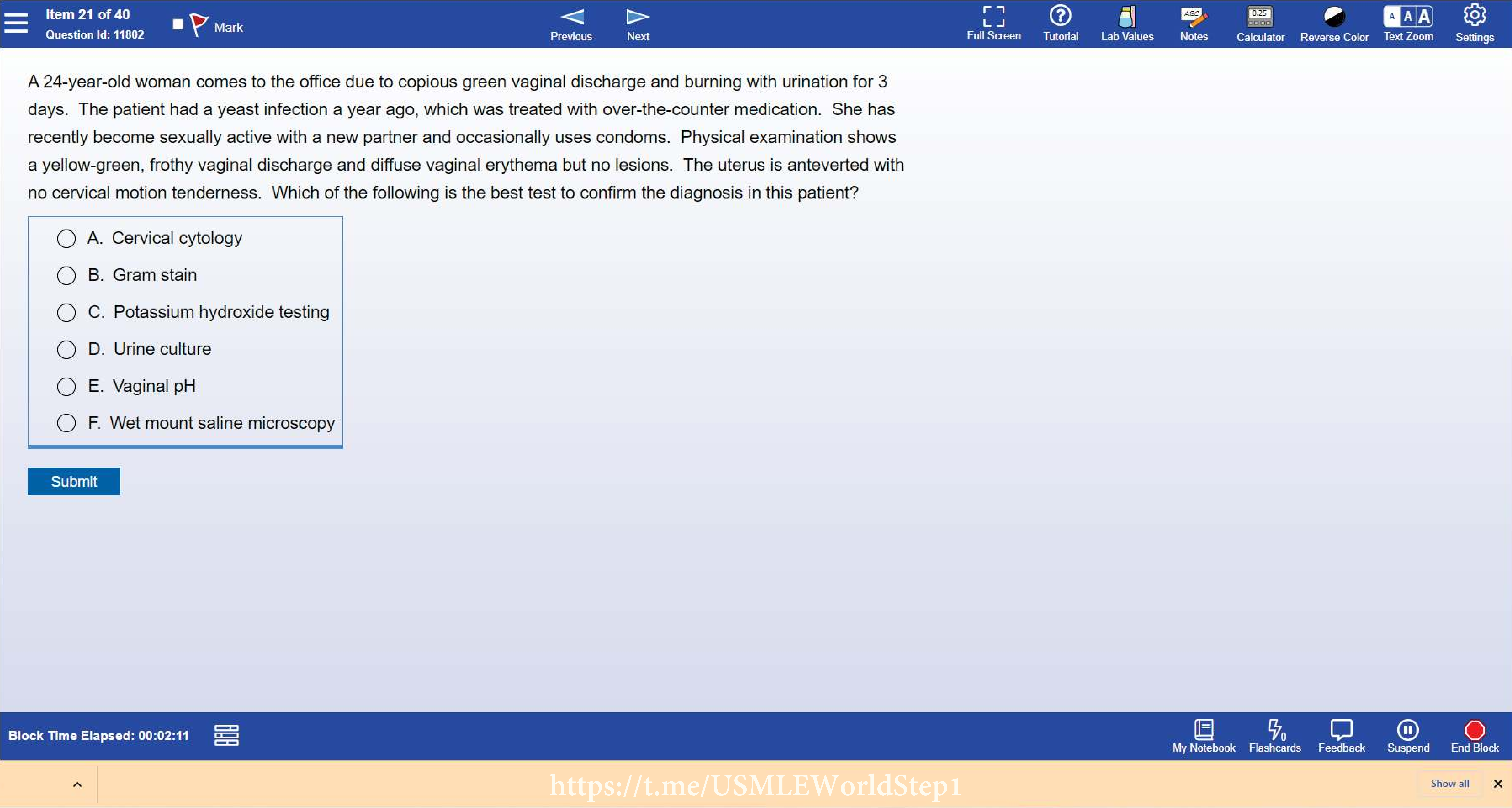
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A 24-year-old woman comes to the office due to copious green vaginal discharge and burning with urination for 3 days. The patient had a yeast infection a year ago, which was treated with over-the-counter medication. She has recently become sexually active with a new partner and occasionally uses condoms. Physical examination shows a yellow-green, frothy vaginal discharge and diffuse vaginal erythema but no lesions. The uterus is anteverted with no cervical motion tenderness. Which of the following is the best test to confirm the diagnosis in this patient?

- ○ A. Cervical cytology
- ○ B. Gram stain
- ○ C. Potassium hydroxide testing
- ○ D. Urine culture
- ○ E. Vaginal pH
- ○ F. Wet mount saline microscopy

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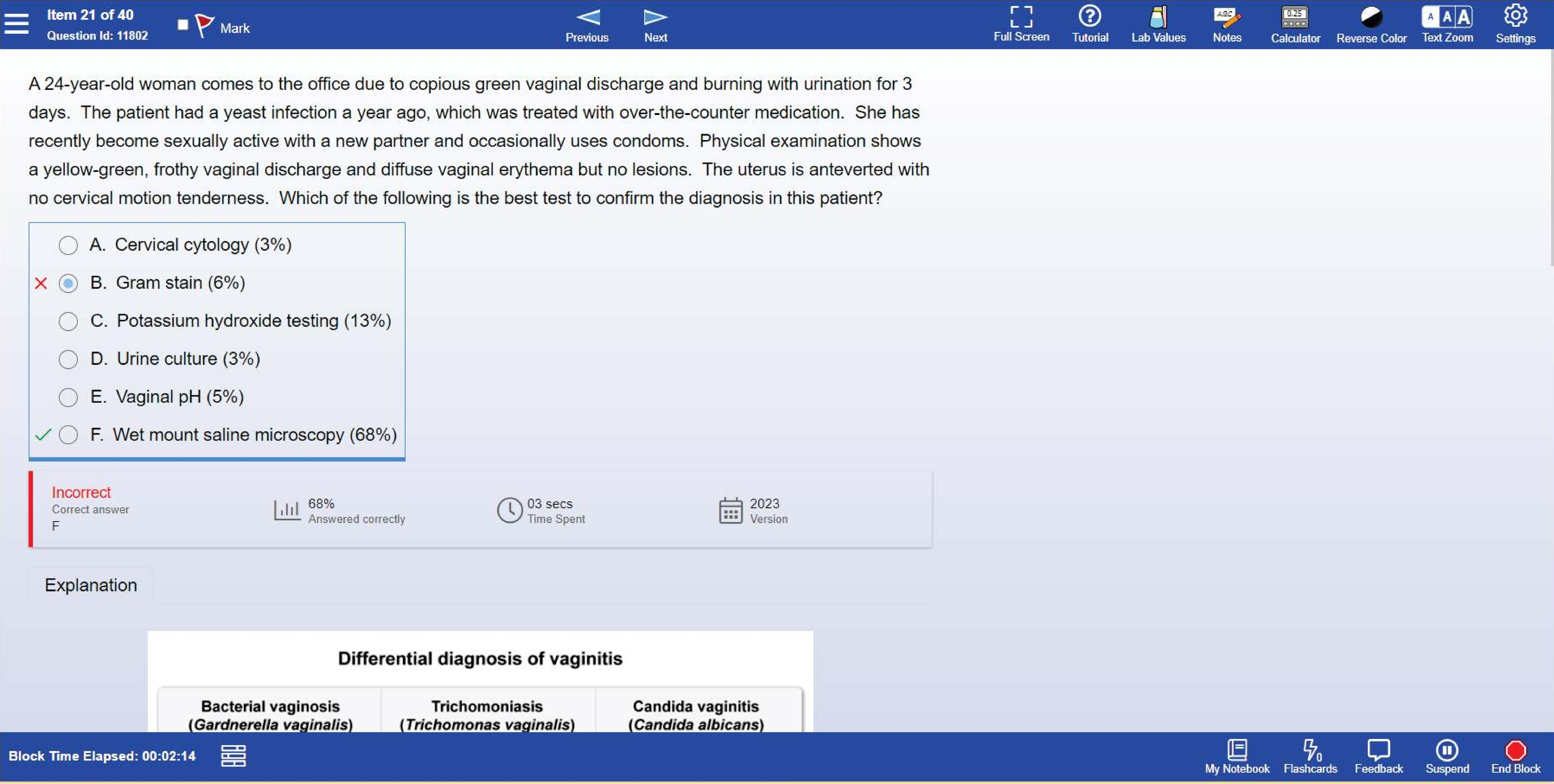
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A 24-year-old woman comes to the office due to copious green vaginal discharge and burning with urination for 3 days. The patient had a yeast infection a year ago, which was treated with over-the-counter medication. She has recently become sexually active with a new partner and occasionally uses condoms. Physical examination shows a yellow-green, frothy vaginal discharge and diffuse vaginal erythema but no lesions. The uterus is anteverted with no cervical motion tenderness. Which of the following is the best test to confirm the diagnosis in this patient?

○ A. Cervical cytology (3%)
✗ ● B. Gram stain (6%)
○ C. Potassium hydroxide testing (13%)
○ D. Urine culture (3%)
○ E. Vaginal pH (5%)
✓ ○ F. Wet mount saline microscopy (68%)

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68%
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Explanation

Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	Trichomoniasis (*Trichomonas vaginalis*)	Candida vaginitis (*Candida albicans*)

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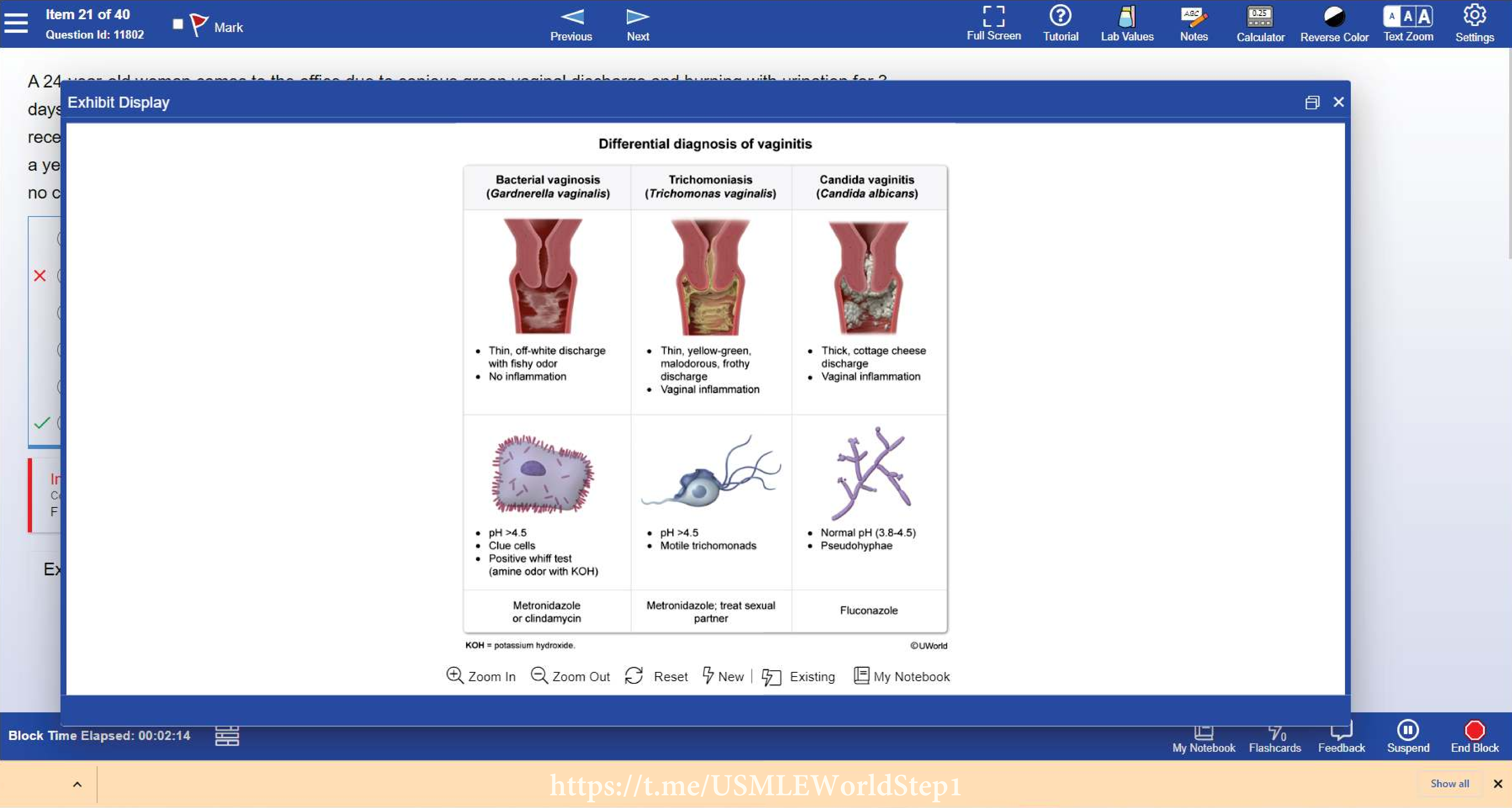
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A 24-year-old woman comes to the office due to copious green vaginal discharge and burning with urination for 3
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Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	Trichomoniasis (*Trichomonas vaginalis*)	Candida vaginitis (*Candida albicans*)
Thin, off-white discharge with fishy odor No inflammation	Thin, yellow-green, malodorous, frothy discharge Vaginal inflammation	Thick, cottage cheese discharge Vaginal inflammation
pH >4.5 Clue cells Positive whiff test (amine odor with KOH)	pH >4.5 Motile trichomonads	Normal pH (3.8-4.5) Pseudohyphae
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

KOH = potassium hydroxide.

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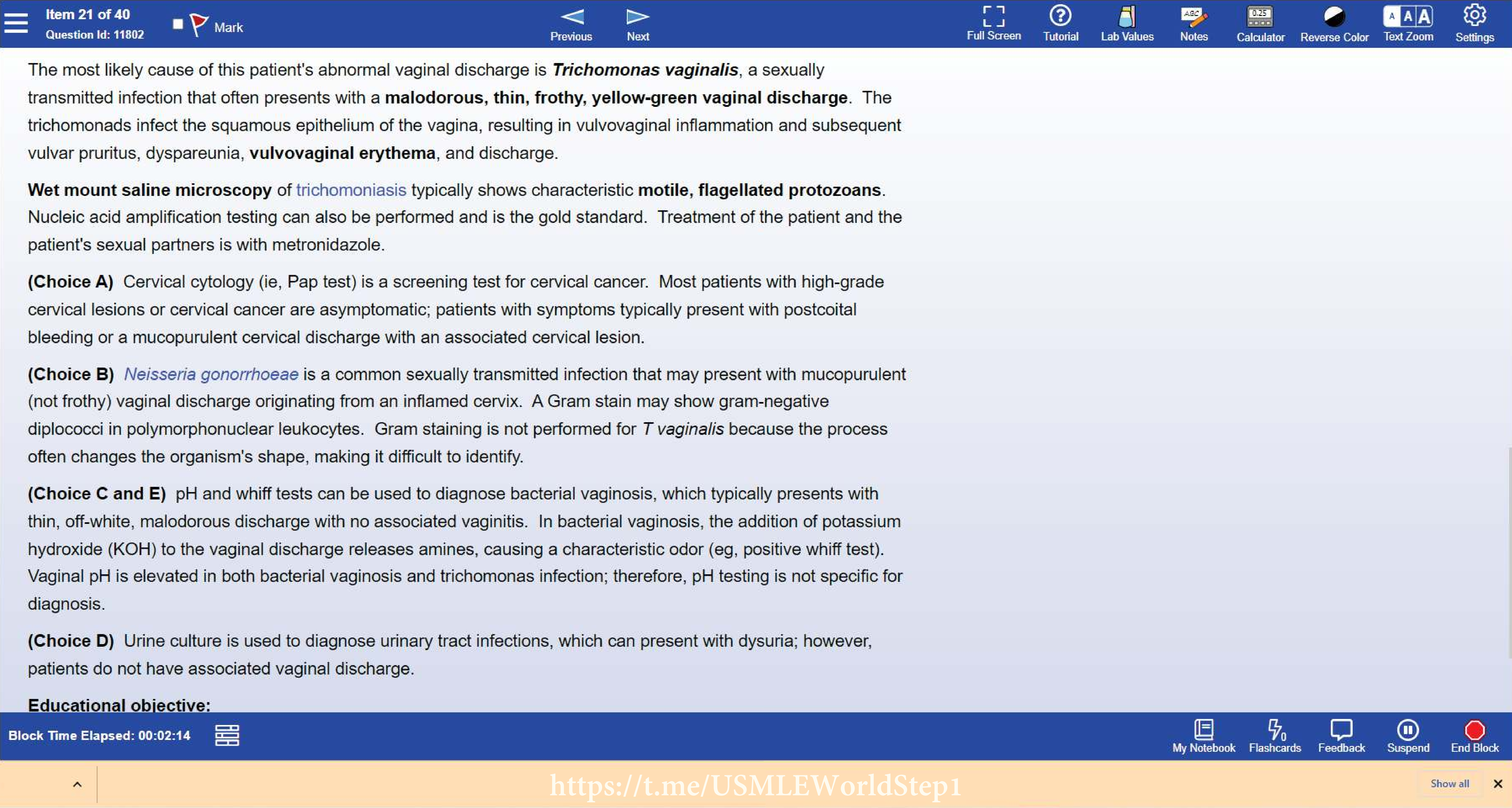


The most likely cause of this patient's abnormal vaginal discharge is ***Trichomonas vaginalis***, a sexually transmitted infection that often presents with a **malodorous, thin, frothy, yellow-green vaginal discharge**. The trichomonads infect the squamous epithelium of the vagina, resulting in vulvovaginal inflammation and subsequent vulvar pruritus, dyspareunia, **vulvovaginal erythema**, and discharge.

Wet mount saline microscopy of trichomoniasis typically shows characteristic **motile, flagellated protozoans**. Nucleic acid amplification testing can also be performed and is the gold standard. Treatment of the patient and the patient's sexual partners is with metronidazole.

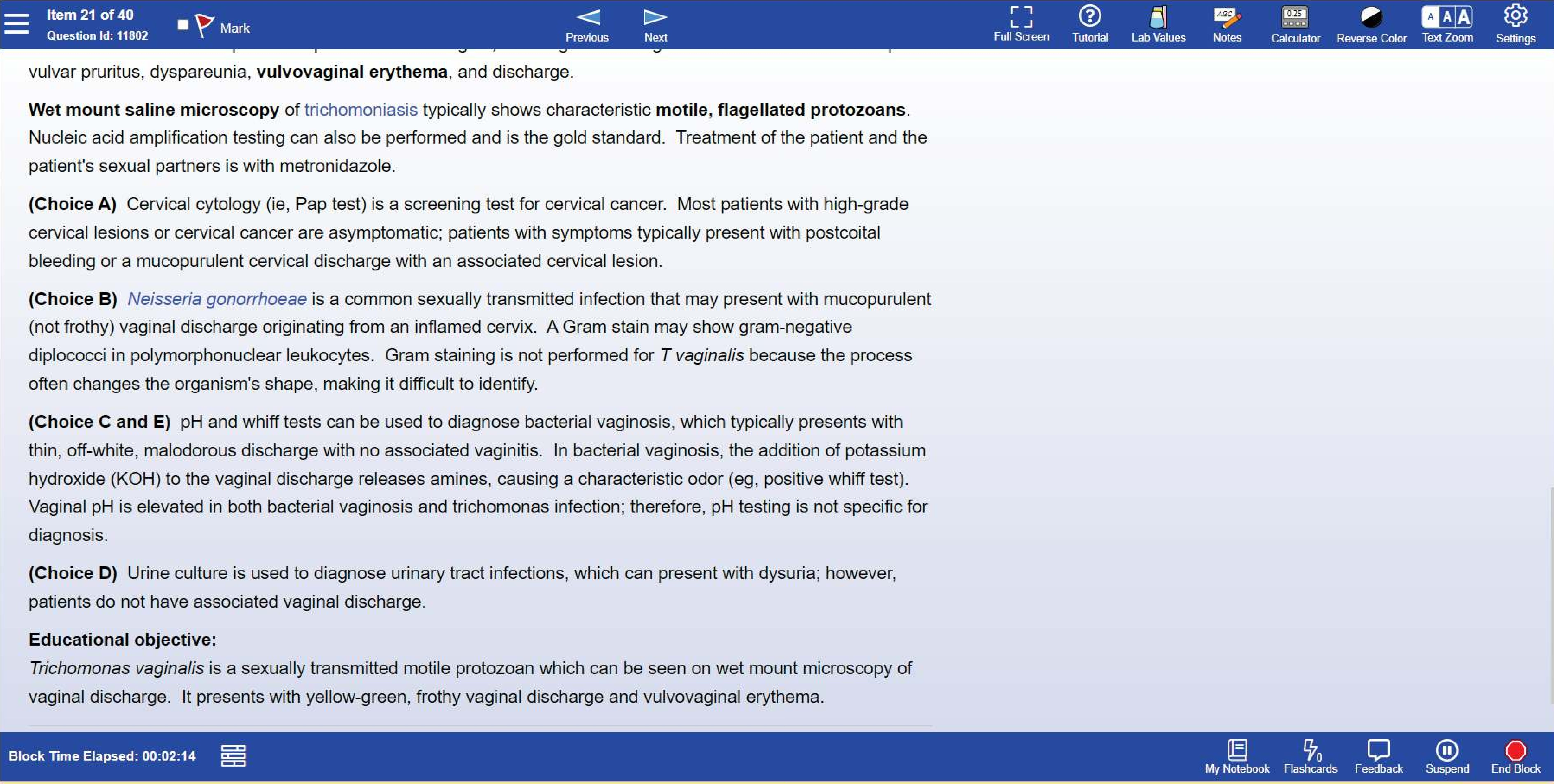
(Choice A) Cervical cytology (ie, Pap test) is a screening test for cervical cancer. Most patients with high-grade cervical lesions or cervical cancer are asymptomatic; patients with symptoms typically present with postcoital bleeding or a mucopurulent cervical discharge with an associated cervical lesion.

(Choice B) *Neisseria gonorrhoeae* is a common sexually transmitted infection that may present with mucopurulent (not frothy) vaginal discharge originating from an inflamed cervix. A Gram stain may show gram-negative diplococci in polymorphonuclear leukocytes. Gram staining is not performed for *T vaginalis* because the process often changes the organism's shape, making it difficult to identify.

(Choice C and E) pH and whiff tests can be used to diagnose bacterial vaginosis, which typically presents with thin, off-white, malodorous discharge with no associated vaginitis. In bacterial vaginosis, the addition of potassium hydroxide (KOH) to the vaginal discharge releases amines, causing a characteristic odor (eg, positive whiff test). Vaginal pH is elevated in both bacterial vaginosis and trichomonas infection; therefore, pH testing is not specific for diagnosis.

(Choice D) Urine culture is used to diagnose urinary tract infections, which can present with dysuria; however, patients do not have associated vaginal discharge.

Educational objective:



vulvar pruritus, dyspareunia, **vulvovaginal erythema**, and discharge.

Wet mount saline microscopy of trichomoniasis typically shows characteristic **motile, flagellated protozoans**. Nucleic acid amplification testing can also be performed and is the gold standard. Treatment of the patient and the patient's sexual partners is with metronidazole.

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(Choice D) Urine culture is used to diagnose urinary tract infections, which can present with dysuria; however, patients do not have associated vaginal discharge.

Educational objective:
Trichomonas vaginalis is a sexually transmitted motile protozoan which can be seen on wet mount microscopy of vaginal discharge. It presents with yellow-green, frothy vaginal discharge and vulvovaginal erythema.

Metronidazole	Metronidazole; treat sexual	Fluconazole

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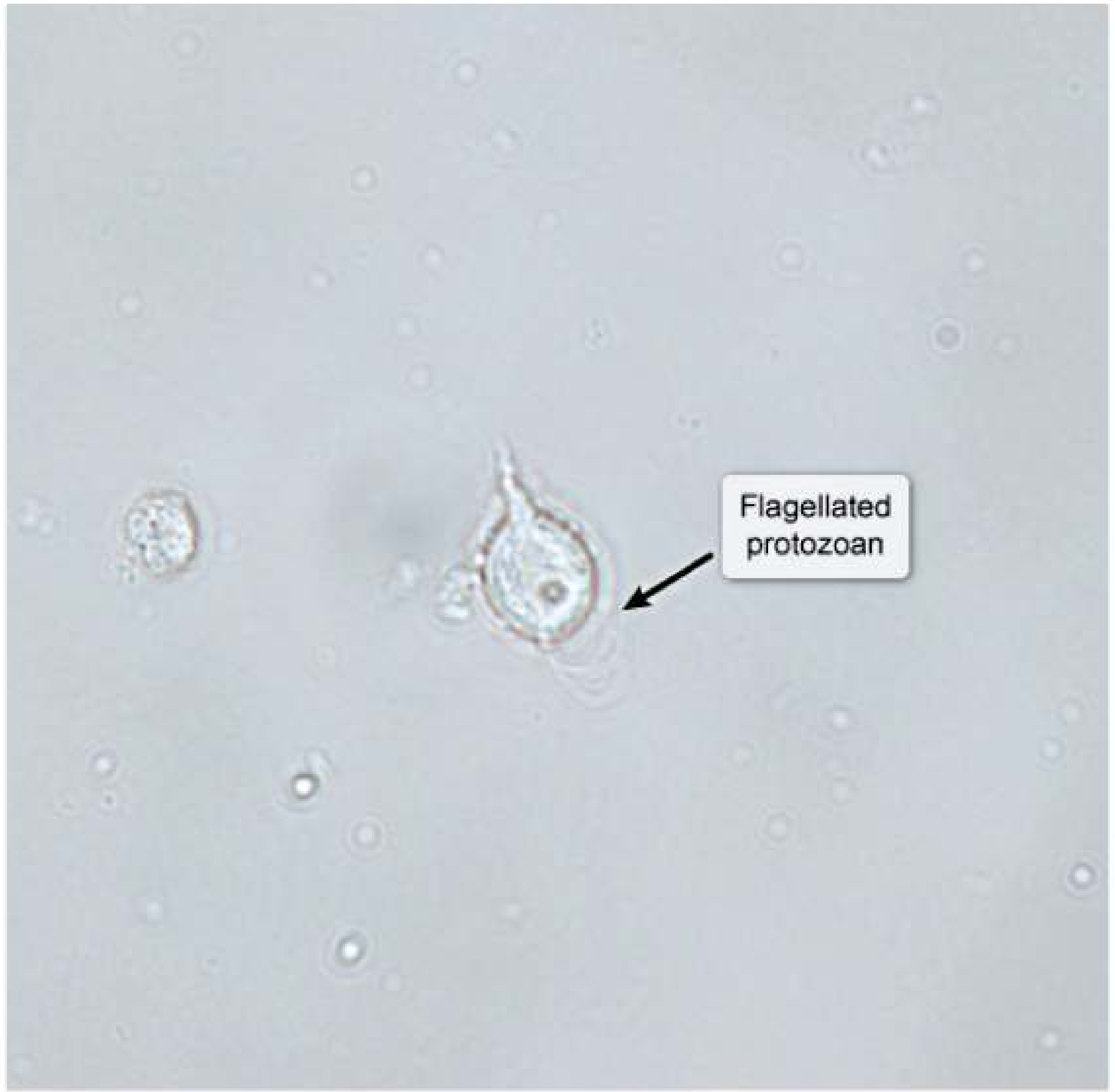
Trichomonas vaginalis


Flagellated protozoan

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Metronidazole	Metronidazole; treat sexual	Fluconazole

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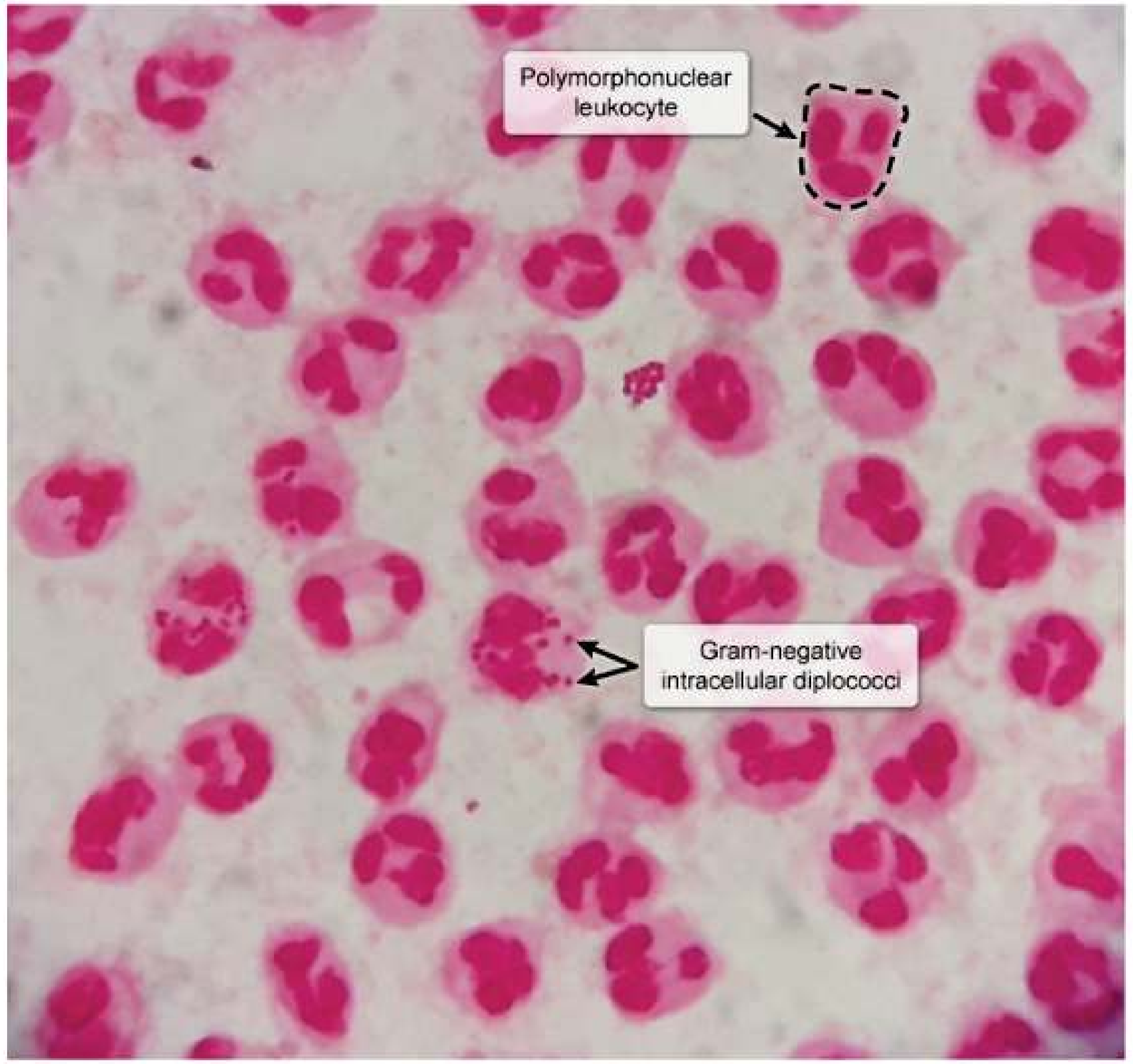
Neisseria gonorrhoeae


Polymorphonuclear leukocyte
Gram-negative intracellular diplococci

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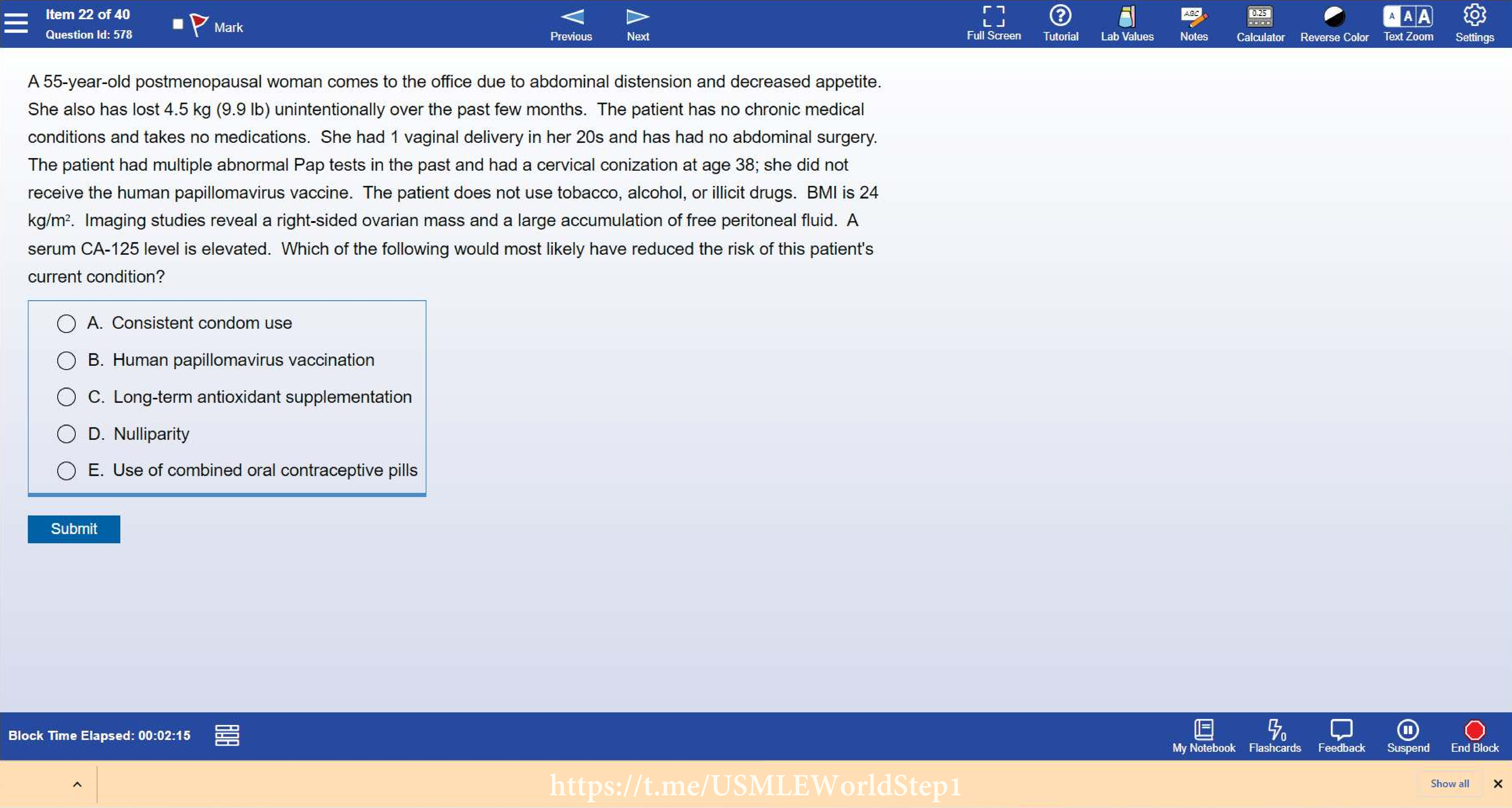
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A 55-year-old postmenopausal woman comes to the office due to abdominal distension and decreased appetite. She also has lost 4.5 kg (9.9 lb) unintentionally over the past few months. The patient has no chronic medical conditions and takes no medications. She had 1 vaginal delivery in her 20s and has had no abdominal surgery. The patient had multiple abnormal Pap tests in the past and had a cervical conization at age 38; she did not receive the human papillomavirus vaccine. The patient does not use tobacco, alcohol, or illicit drugs. BMI is 24 kg/m^2. Imaging studies reveal a right-sided ovarian mass and a large accumulation of free peritoneal fluid. A serum CA-125 level is elevated. Which of the following would most likely have reduced the risk of this patient's current condition?

- ○ A. Consistent condom use
- ○ B. Human papillomavirus vaccination
- ○ C. Long-term antioxidant supplementation
- ○ D. Nulliparity
- ○ E. Use of combined oral contraceptive pills

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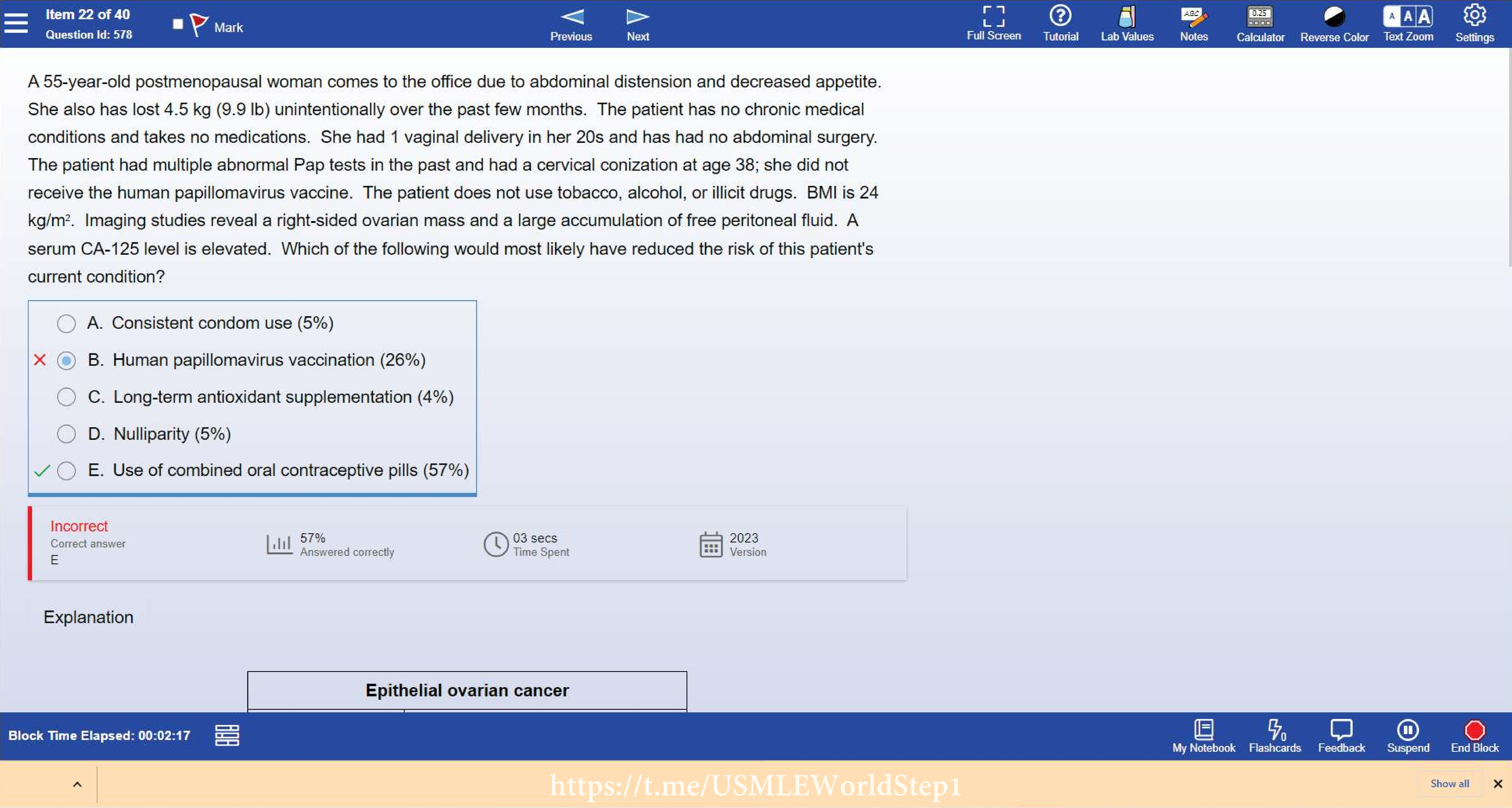
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○ A. Consistent condom use (5%)

✗ ● B. Human papillomavirus vaccination (26%)

○ C. Long-term antioxidant supplementation (4%)

○ D. Nulliparity (5%)

✓ ○ E. Use of combined oral contraceptive pills (57%)

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Correct answer
E

57%
Answered correctly

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Explanation

Epithelial ovarian cancer

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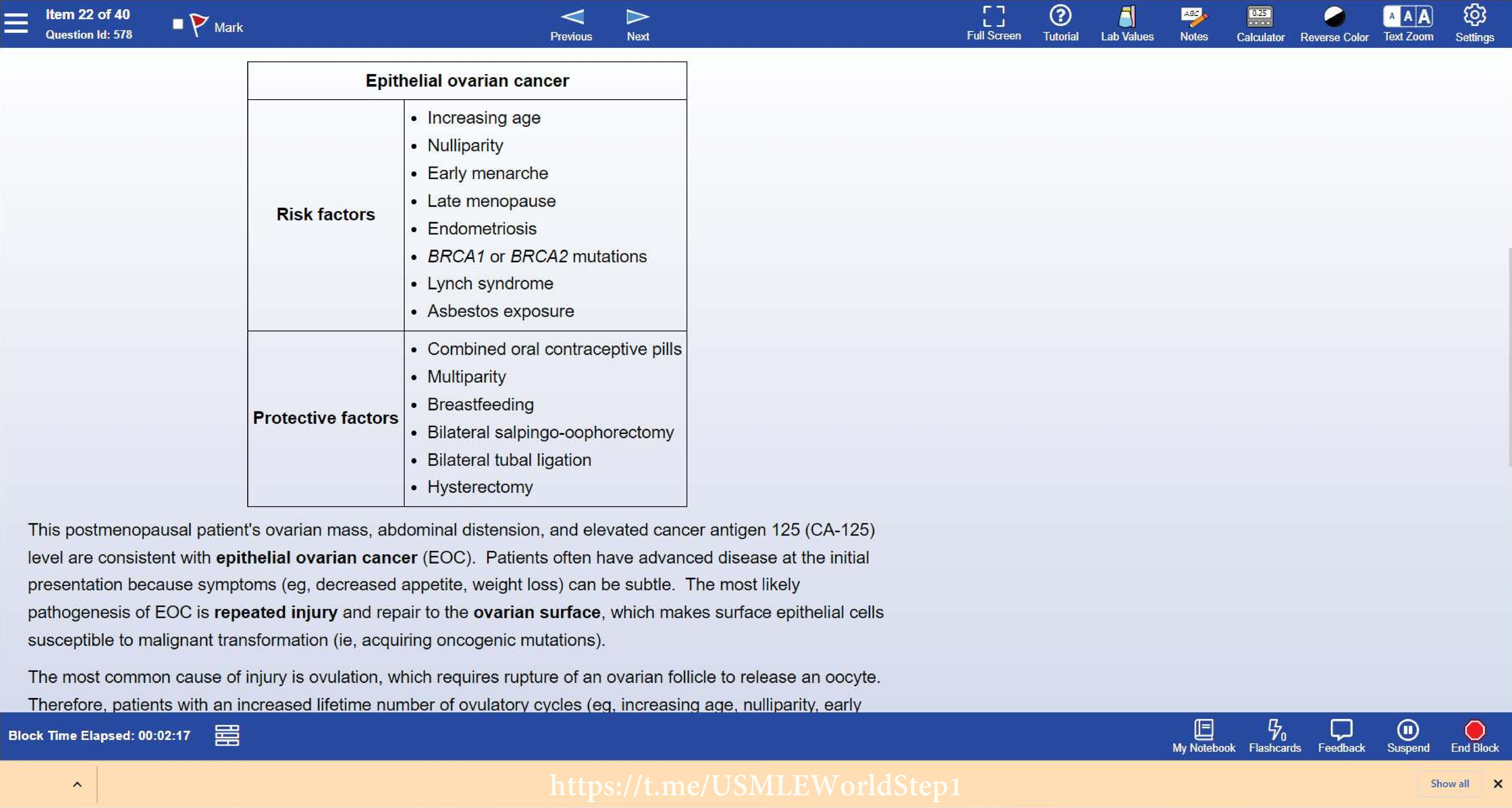
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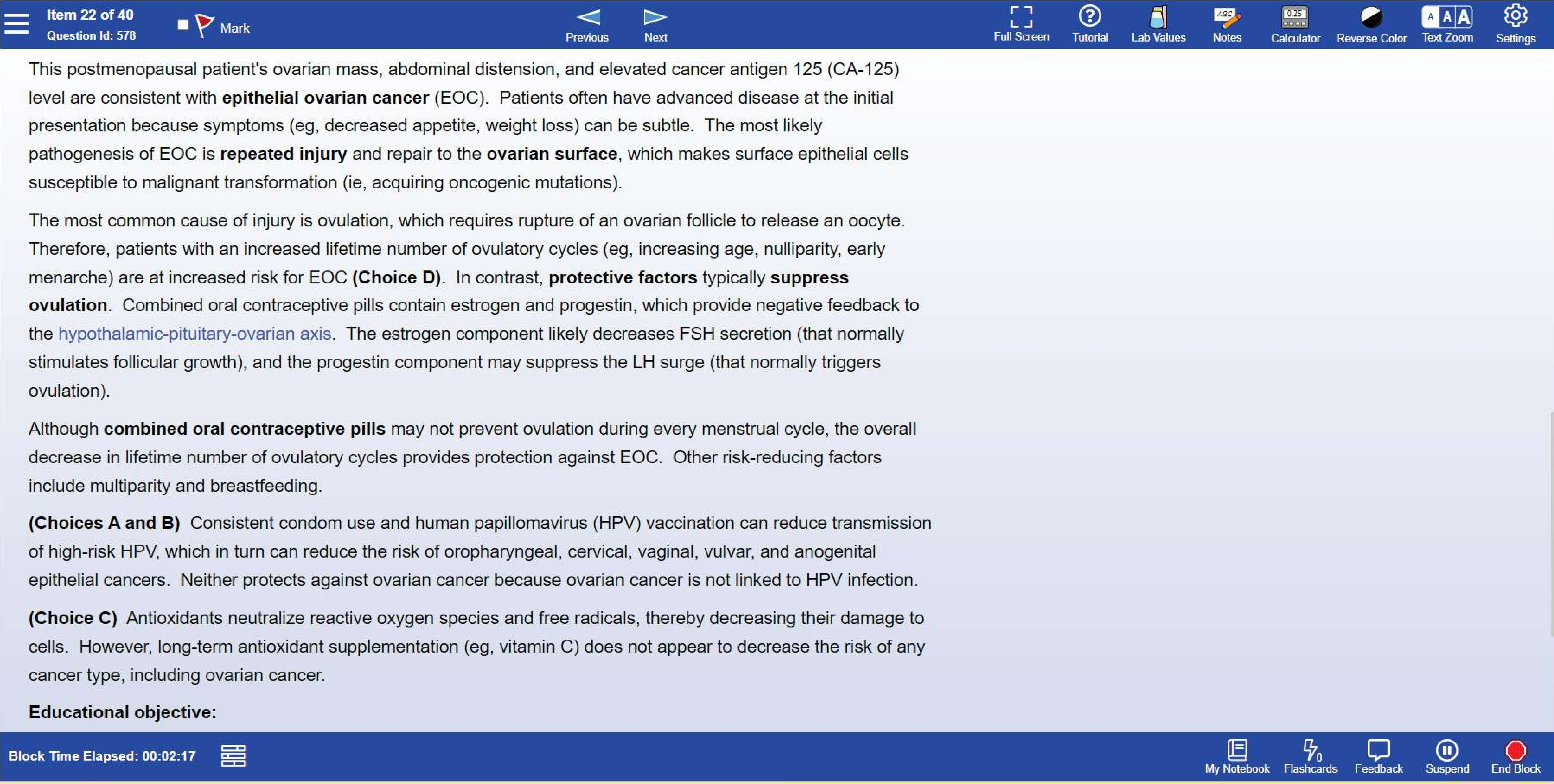
Epithelial ovarian cancer	
Risk factors	• Increasing age • Nulliparity • Early menarche • Late menopause • Endometriosis • *BRCA1* or *BRCA2* mutations • Lynch syndrome • Asbestos exposure
Protective factors	• Combined oral contraceptive pills • Multiparity • Breastfeeding • Bilateral salpingo-oophorectomy • Bilateral tubal ligation • Hysterectomy

This postmenopausal patient's ovarian mass, abdominal distension, and elevated cancer antigen 125 (CA-125) level are consistent with **epithelial ovarian cancer** (EOC). Patients often have advanced disease at the initial presentation because symptoms (eg, decreased appetite, weight loss) can be subtle. The most likely pathogenesis of EOC is **repeated injury** and repair to the **ovarian surface**, which makes surface epithelial cells susceptible to malignant transformation (ie, acquiring oncogenic mutations).

The most common cause of injury is ovulation, which requires rupture of an ovarian follicle to release an oocyte. Therefore, patients with an increased lifetime number of ovulatory cycles (eg, increasing age, nulliparity, early



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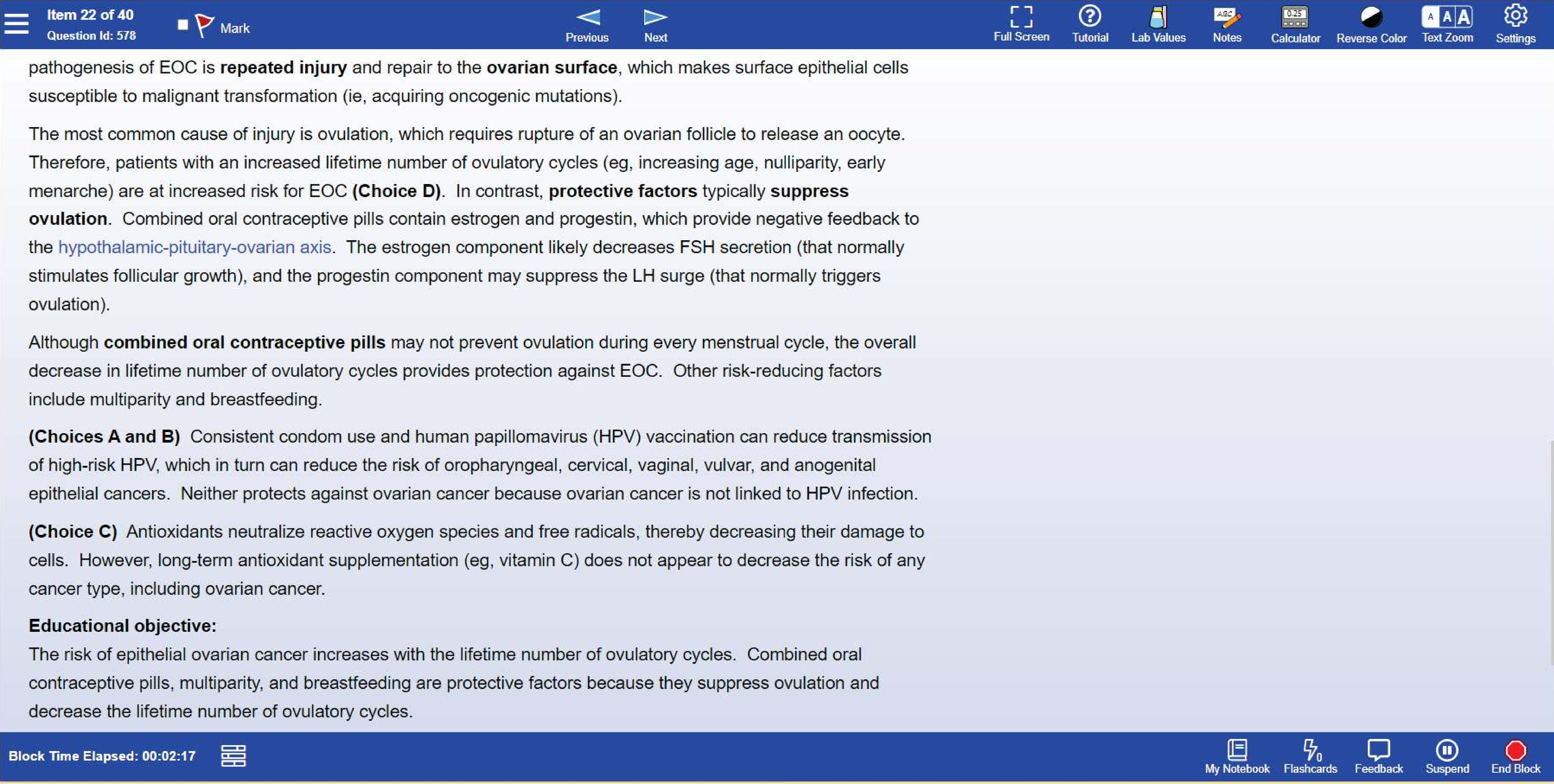
The most common cause of injury is ovulation, which requires rupture of an ovarian follicle to release an oocyte. Therefore, patients with an increased lifetime number of ovulatory cycles (eg, increasing age, nulliparity, early menarche) are at increased risk for EOC **(Choice D)**. In contrast, **protective factors** typically **suppress ovulation**. Combined oral contraceptive pills contain estrogen and progestin, which provide negative feedback to the hypothalamic-pituitary-ovarian axis. The estrogen component likely decreases FSH secretion (that normally stimulates follicular growth), and the progestin component may suppress the LH surge (that normally triggers ovulation).

Although **combined oral contraceptive pills** may not prevent ovulation during every menstrual cycle, the overall decrease in lifetime number of ovulatory cycles provides protection against EOC. Other risk-reducing factors include multiparity and breastfeeding.

(Choices A and B) Consistent condom use and human papillomavirus (HPV) vaccination can reduce transmission of high-risk HPV, which in turn can reduce the risk of oropharyngeal, cervical, vaginal, vulvar, and anogenital epithelial cancers. Neither protects against ovarian cancer because ovarian cancer is not linked to HPV infection.

(Choice C) Antioxidants neutralize reactive oxygen species and free radicals, thereby decreasing their damage to cells. However, long-term antioxidant supplementation (eg, vitamin C) does not appear to decrease the risk of any cancer type, including ovarian cancer.

Educational objective:



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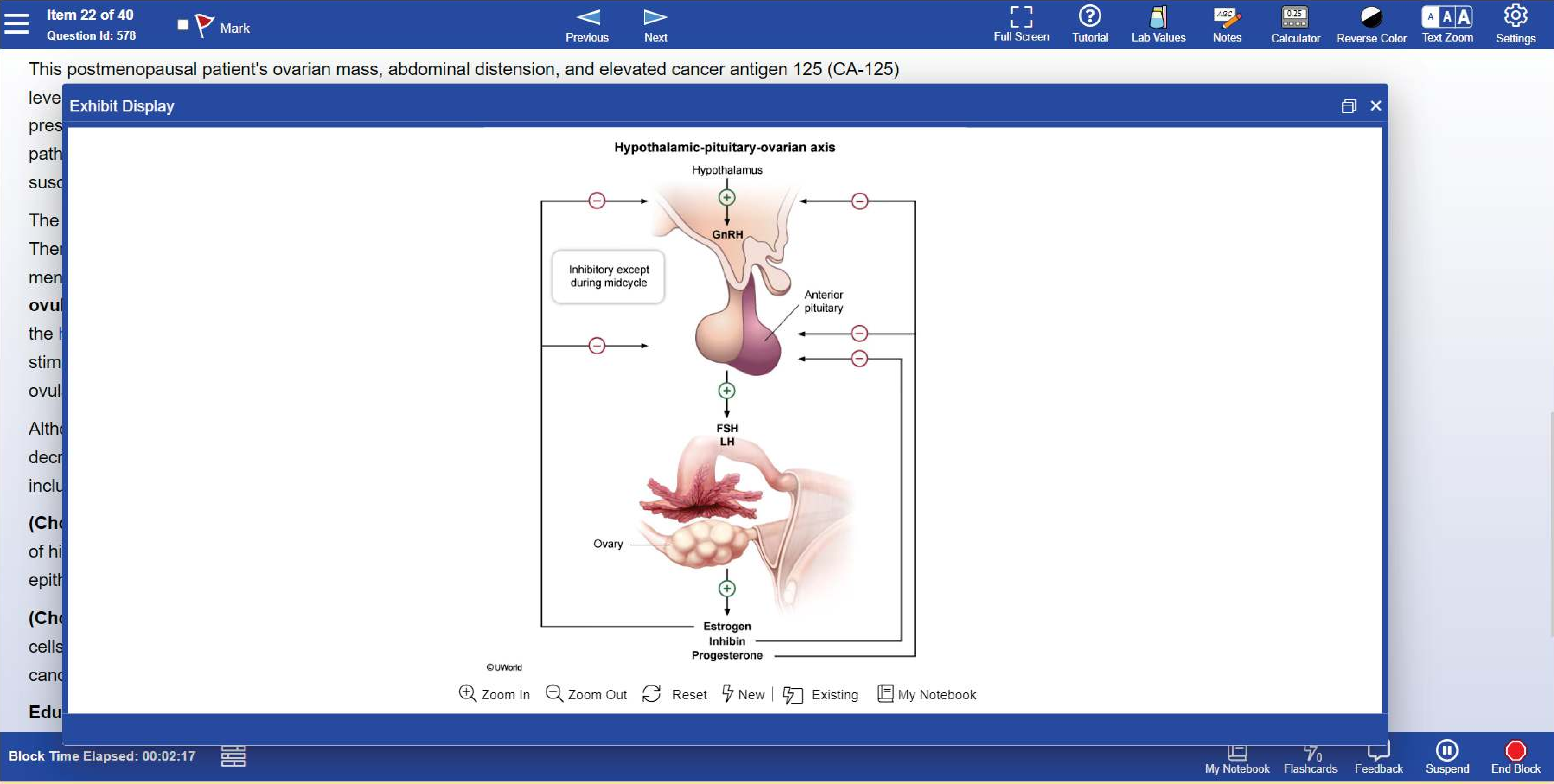
(Choice C) Antioxidants neutralize reactive oxygen species and free radicals, thereby decreasing their damage to cells. However, long-term antioxidant supplementation (eg, vitamin C) does not appear to decrease the risk of any cancer type, including ovarian cancer.

Educational objective:

The risk of epithelial ovarian cancer increases with the lifetime number of ovulatory cycles. Combined oral contraceptive pills, multiparity, and breastfeeding are protective factors because they suppress ovulation and decrease the lifetime number of ovulatory cycles.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Hypothalamus
GnRH
Inhibitory except during midcycle
Anterior pituitary
FSH
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This postmenopausal patient's ovarian mass, abdominal distension, and elevated cancer antigen 125 (CA-125)

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Hypothalamic-pituitary-ovarian axis

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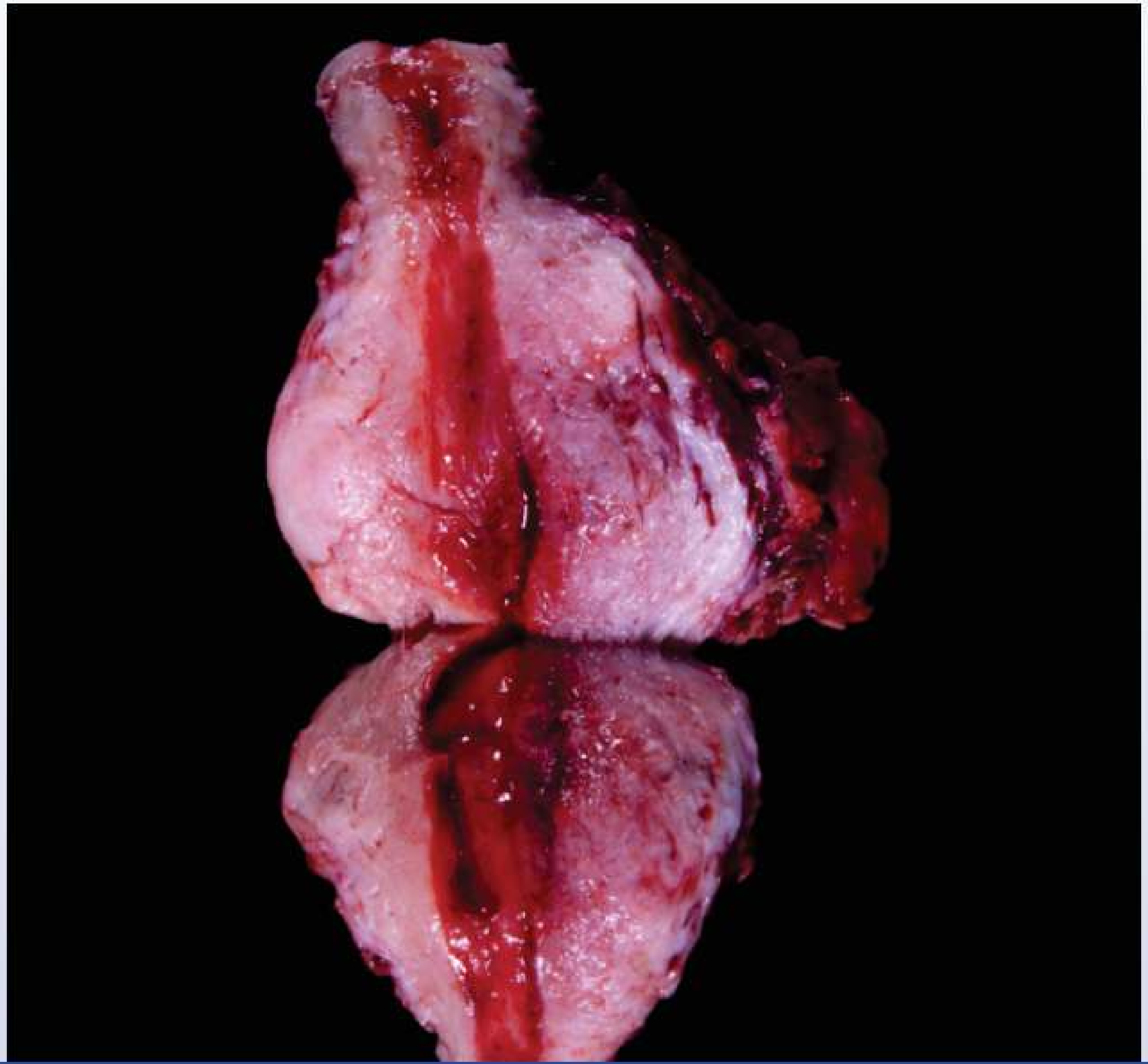
A 48-year-old woman comes to the office due to painful, heavy menses for the past 6 months. The patient has 4-5 days of heavy bleeding, often soaking through a tampon or sanitary napkin every few hours. Menstrual periods occur every 28-30 days. The patient is not on contraception and has no significant medical history. Vital signs are normal. Urine pregnancy test is negative. After an appropriate workup, a hysterectomy is performed, and the surgical specimen is shown below:



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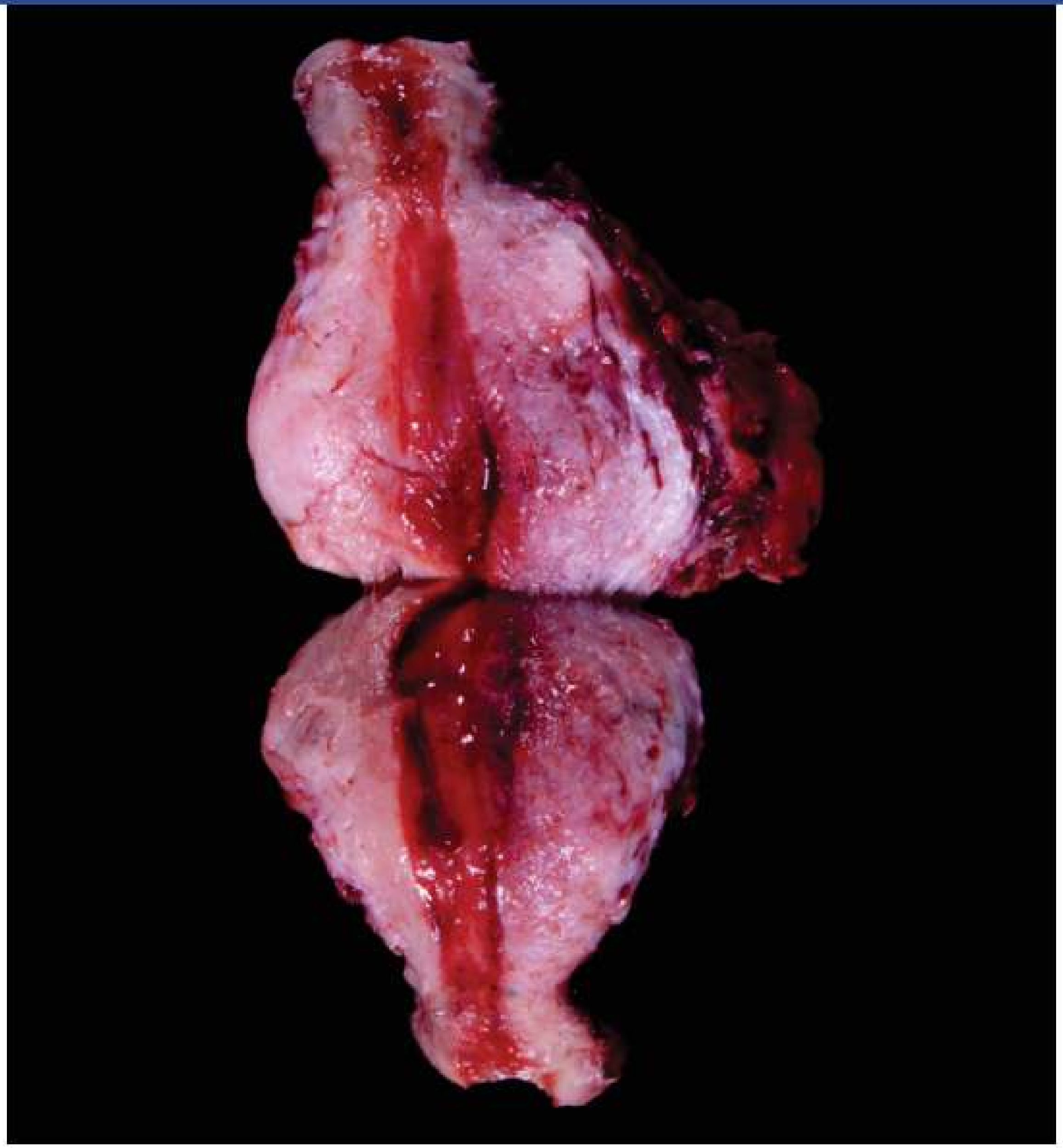

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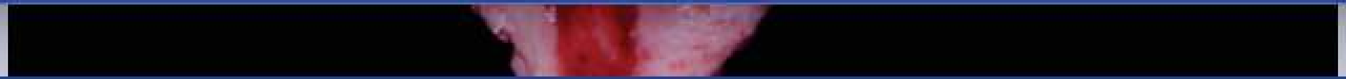

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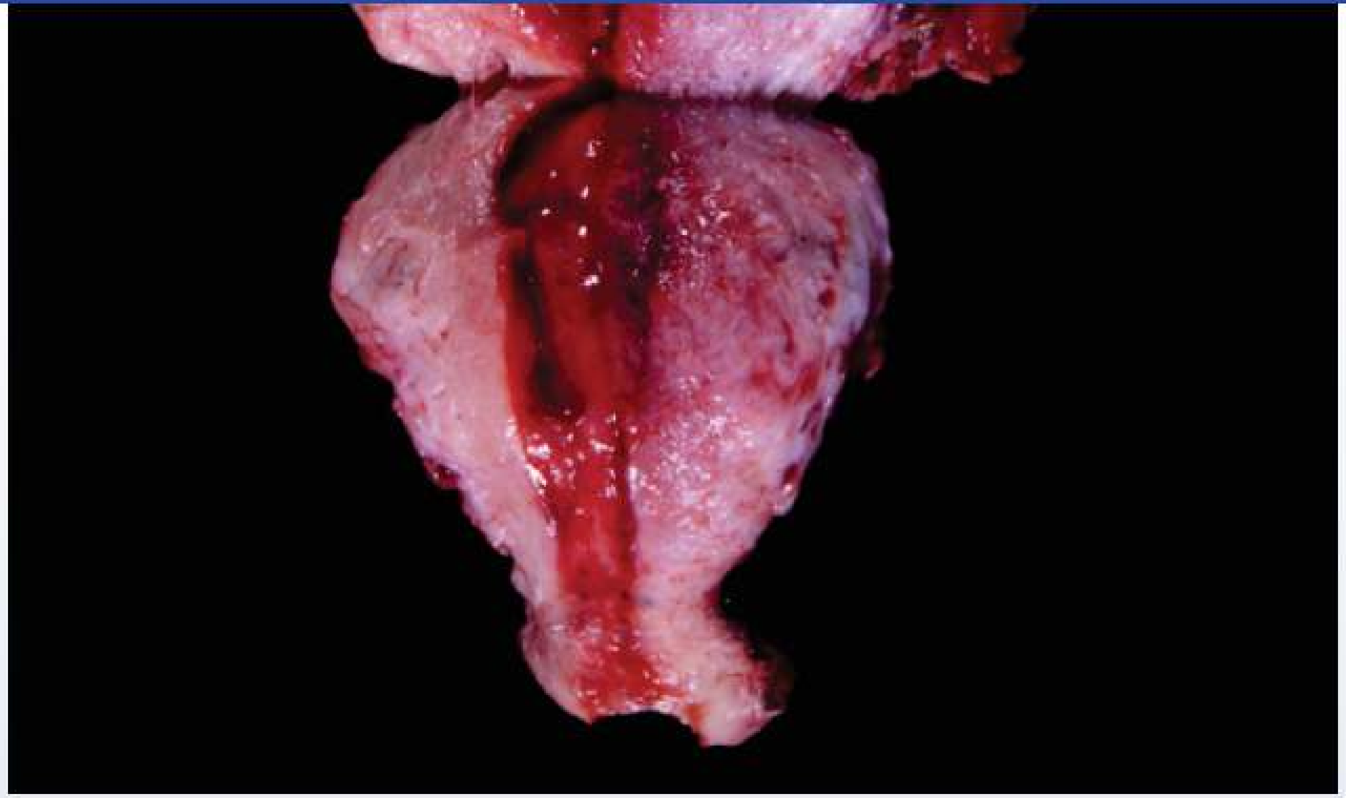

Which of the following is the most likely diagnosis?

- ○ A. Adenomyosis
- ○ B. Chronic endometritis
- ○ C. Complete hydatidiform mole
- ○ D. Endometriosis
- ○ E. Uterine leiomyoma
- ○ F. Uterine sarcoma

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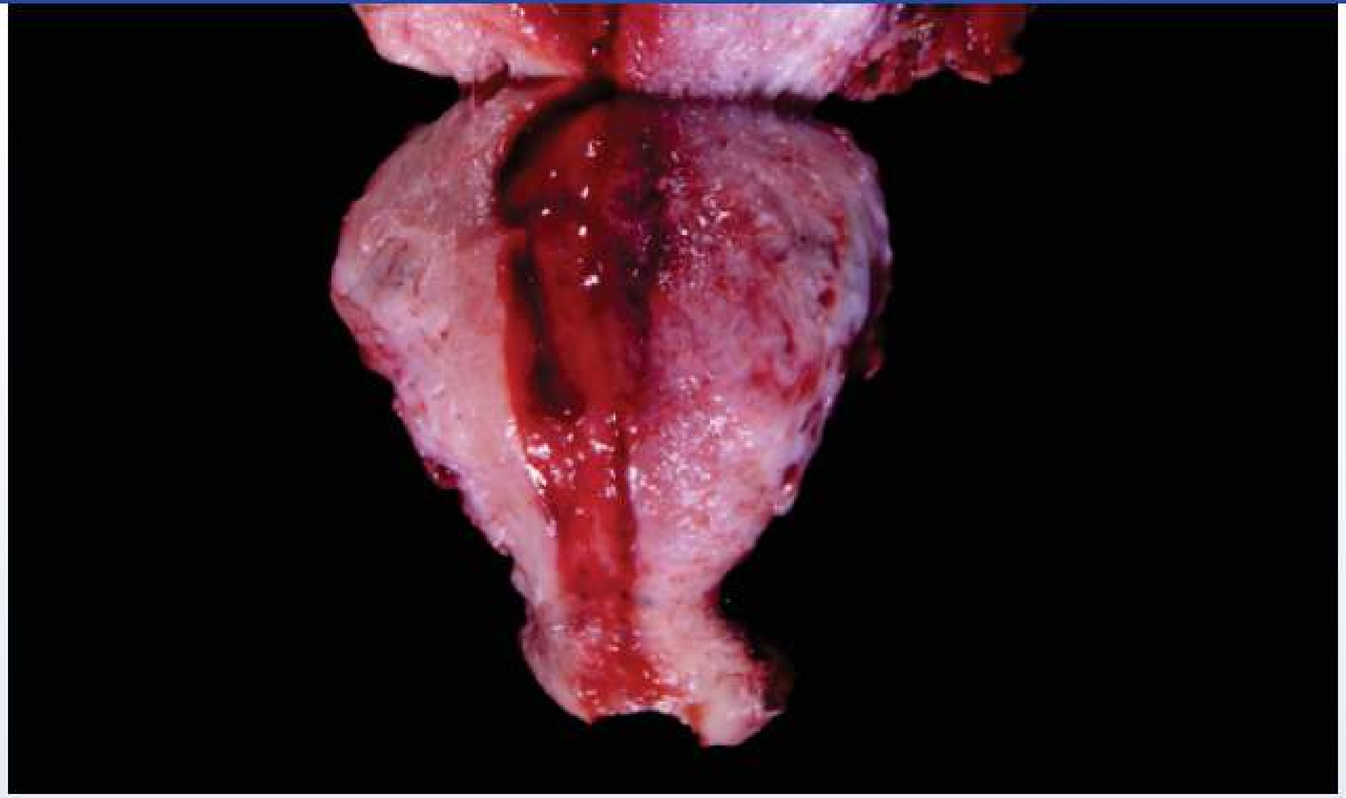

Which of the following is the most likely diagnosis?

- ✓ ○ A. Adenomyosis (50%)
- ○ B. Chronic endometritis (5%)
- ○ C. Complete hydatidiform mole (0%)
- ✗ ● D. Endometriosis (11%)
- ○ E. Uterine leiomyoma (21%)
- ○ F. Uterine sarcoma (10%)

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Correct answer
A

50%
Answered correctly

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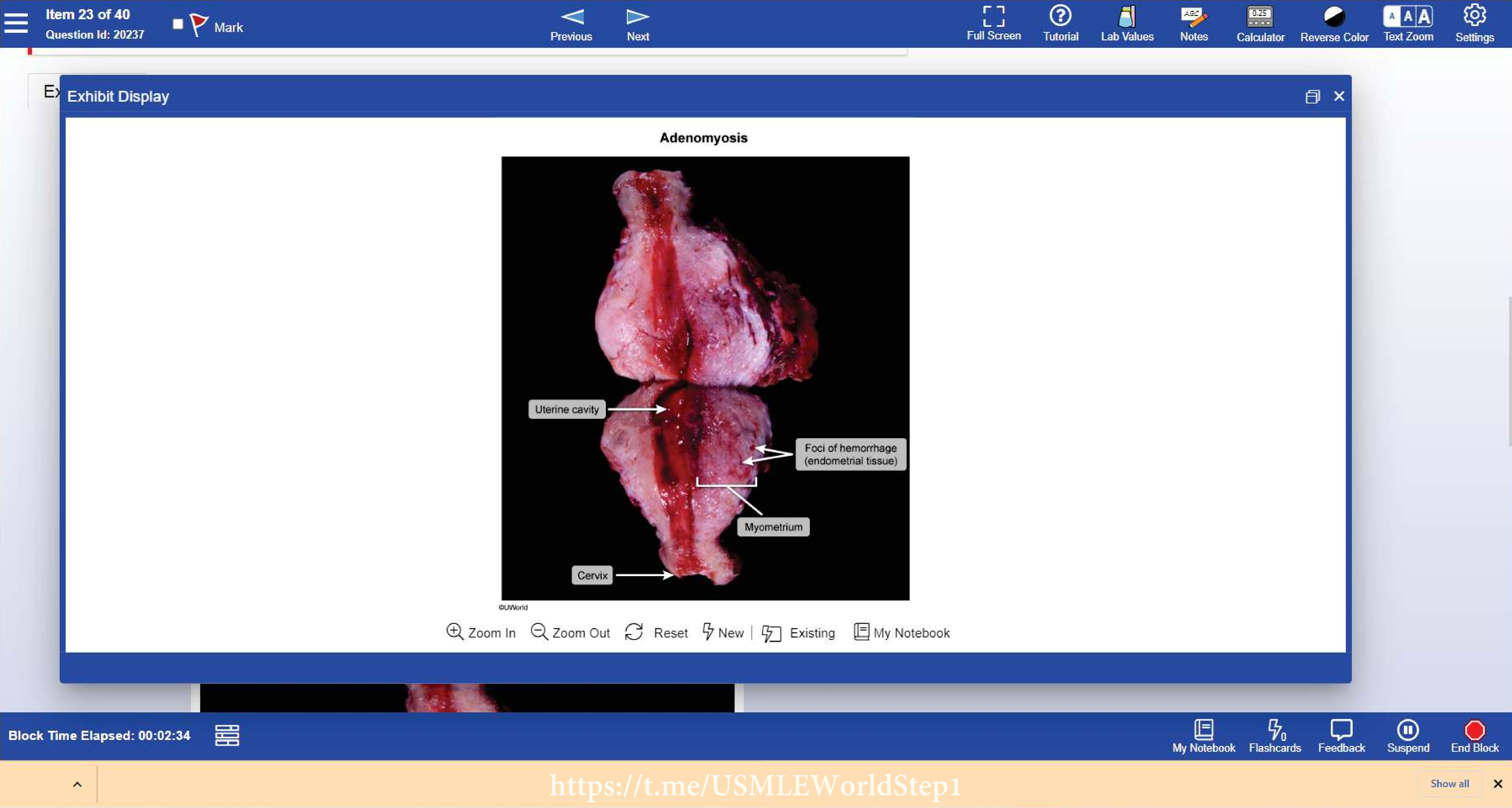
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Adenomyosis

Uterine cavity
Foci of hemorrhage (endometrial tissue)
Myometrium
Cervix

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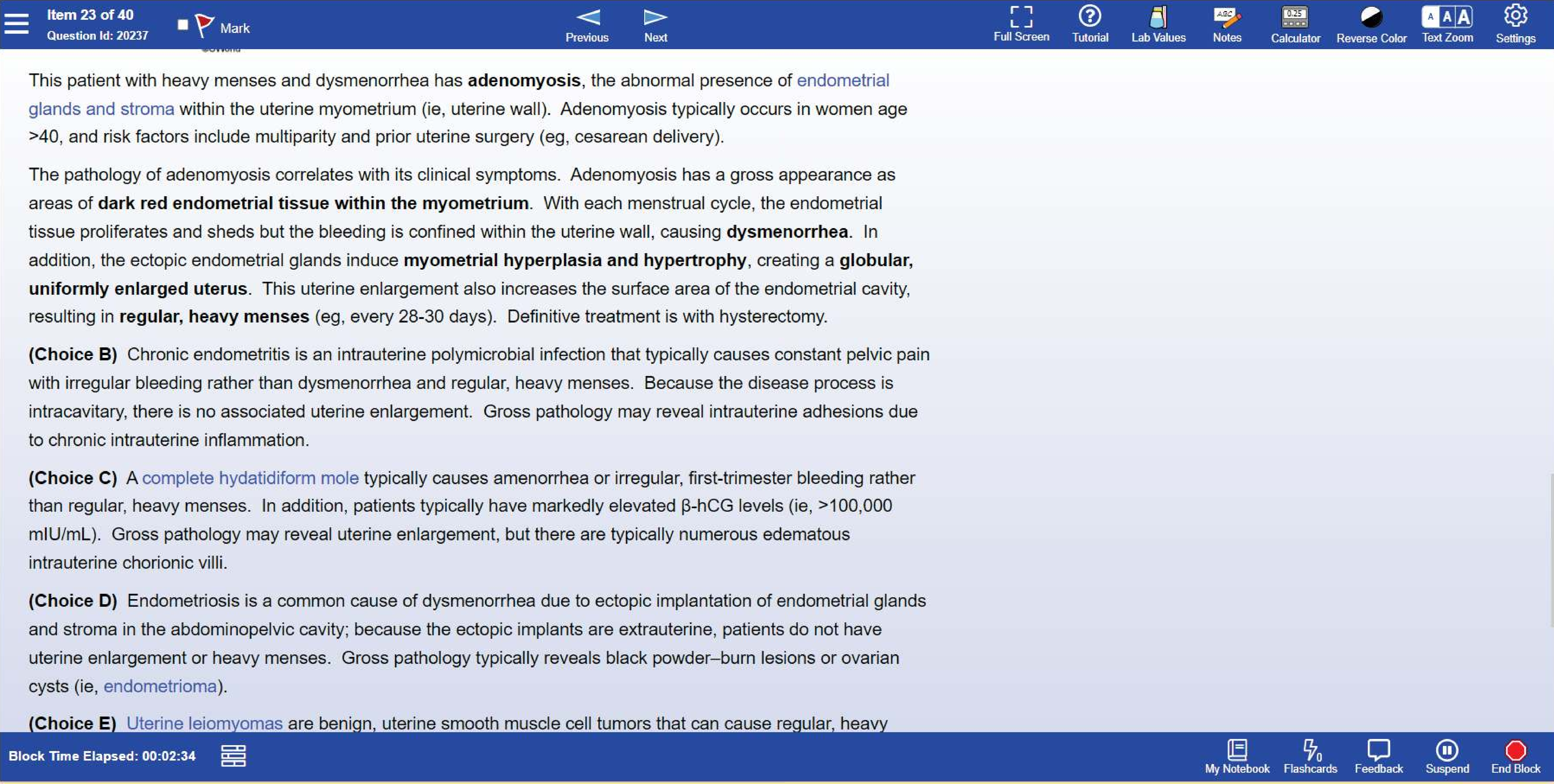


This patient with heavy menses and dysmenorrhea has **adenomyosis**, the abnormal presence of endometrial glands and stroma within the uterine myometrium (ie, uterine wall). Adenomyosis typically occurs in women age >40, and risk factors include multiparity and prior uterine surgery (eg, cesarean delivery).

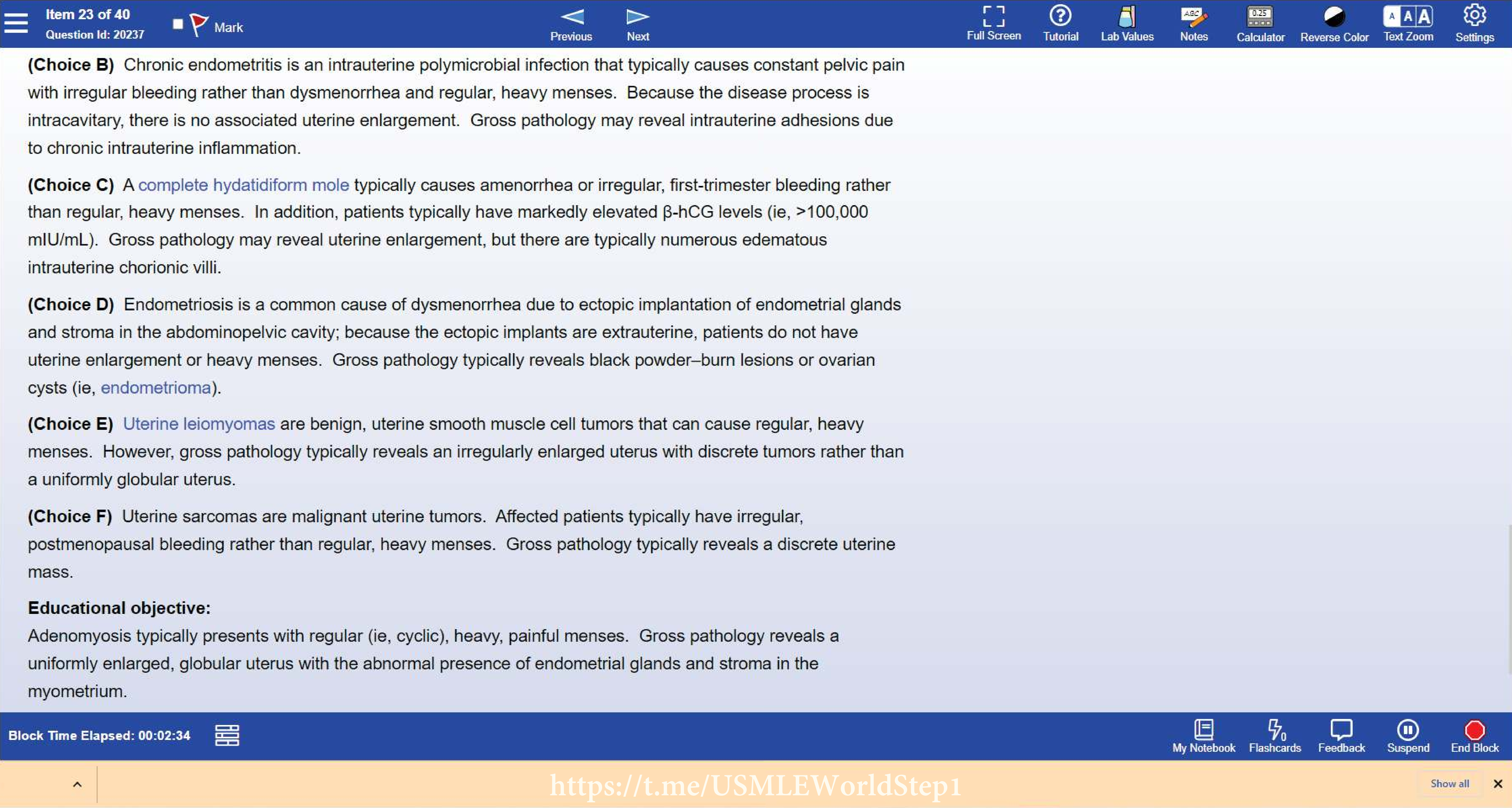
The pathology of adenomyosis correlates with its clinical symptoms. Adenomyosis has a gross appearance as areas of **dark red endometrial tissue within the myometrium**. With each menstrual cycle, the endometrial tissue proliferates and sheds but the bleeding is confined within the uterine wall, causing **dysmenorrhea**. In addition, the ectopic endometrial glands induce **myometrial hyperplasia and hypertrophy**, creating a **globular, uniformly enlarged uterus**. This uterine enlargement also increases the surface area of the endometrial cavity, resulting in **regular, heavy menses** (eg, every 28-30 days). Definitive treatment is with hysterectomy.

(Choice B) Chronic endometritis is an intrauterine polymicrobial infection that typically causes constant pelvic pain with irregular bleeding rather than dysmenorrhea and regular, heavy menses. Because the disease process is intracavitary, there is no associated uterine enlargement. Gross pathology may reveal intrauterine adhesions due to chronic intrauterine inflammation.

(Choice C) A complete hydatidiform mole typically causes amenorrhea or irregular, first-trimester bleeding rather than regular, heavy menses. In addition, patients typically have markedly elevated β-hCG levels (ie, >100,000 mIU/mL). Gross pathology may reveal uterine enlargement, but there are typically numerous edematous intrauterine chorionic villi.

(Choice D) Endometriosis is a common cause of dysmenorrhea due to ectopic implantation of endometrial glands and stroma in the abdominopelvic cavity; because the ectopic implants are extrauterine, patients do not have uterine enlargement or heavy menses. Gross pathology typically reveals black powder–burn lesions or ovarian cysts (ie, endometrioma).

(Choice E) Uterine leiomyomas are benign, uterine smooth muscle cell tumors that can cause regular, heavy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(Choice E) Uterine leiomyomas are benign, uterine smooth muscle cell tumors that can cause regular, heavy menses. However, gross pathology typically reveals an irregularly enlarged uterus with discrete tumors rather than a uniformly globular uterus.

(Choice F) Uterine sarcomas are malignant uterine tumors. Affected patients typically have irregular, postmenopausal bleeding rather than regular, heavy menses. Gross pathology typically reveals a discrete uterine mass.

Educational objective:

Adenomyosis typically presents with regular (ie, cyclic), heavy, painful menses. Gross pathology reveals a uniformly enlarged, globular uterus with the abnormal presence of endometrial glands and stroma in the myometrium.

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Cervix

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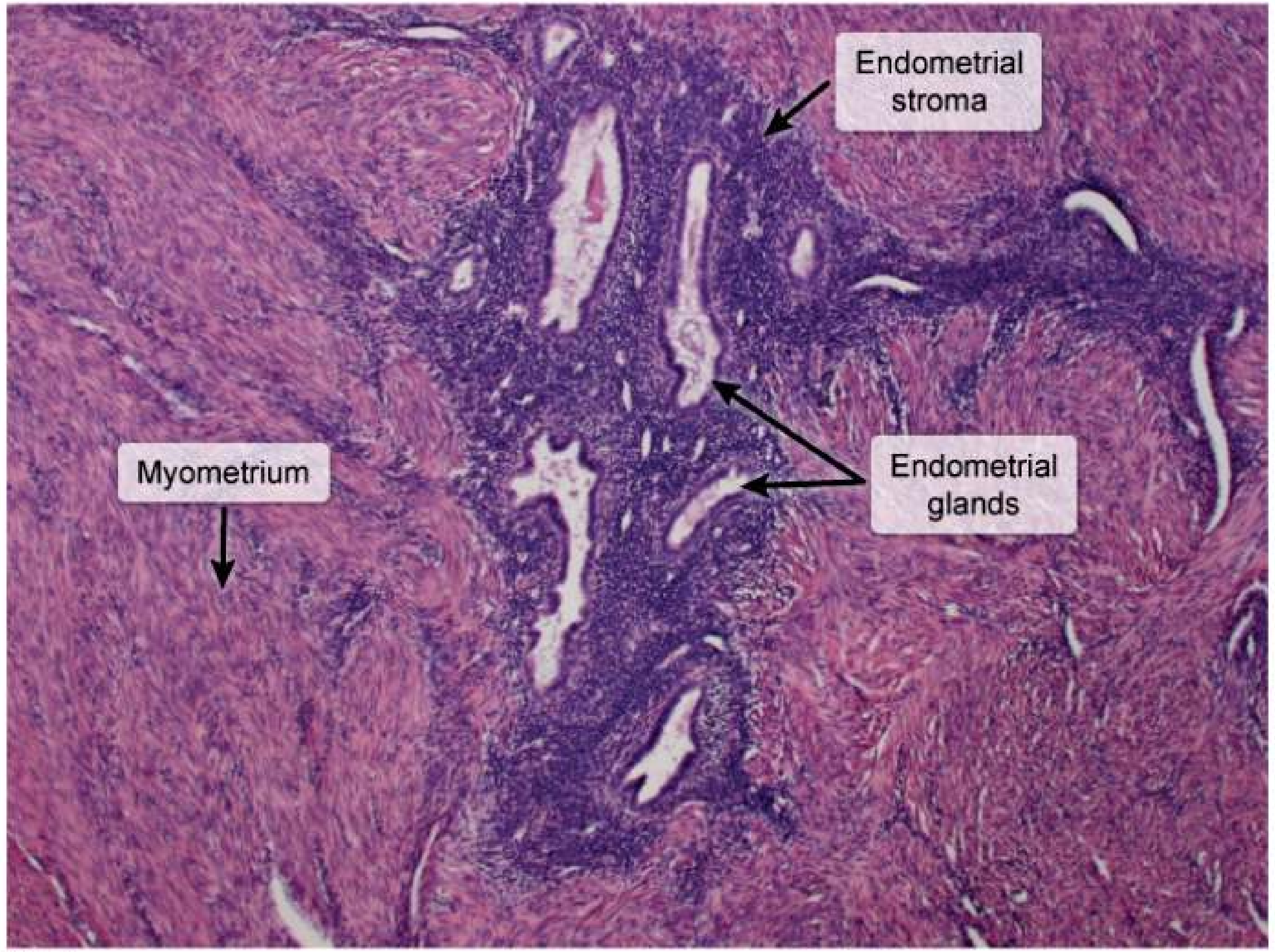
Adenomyosis



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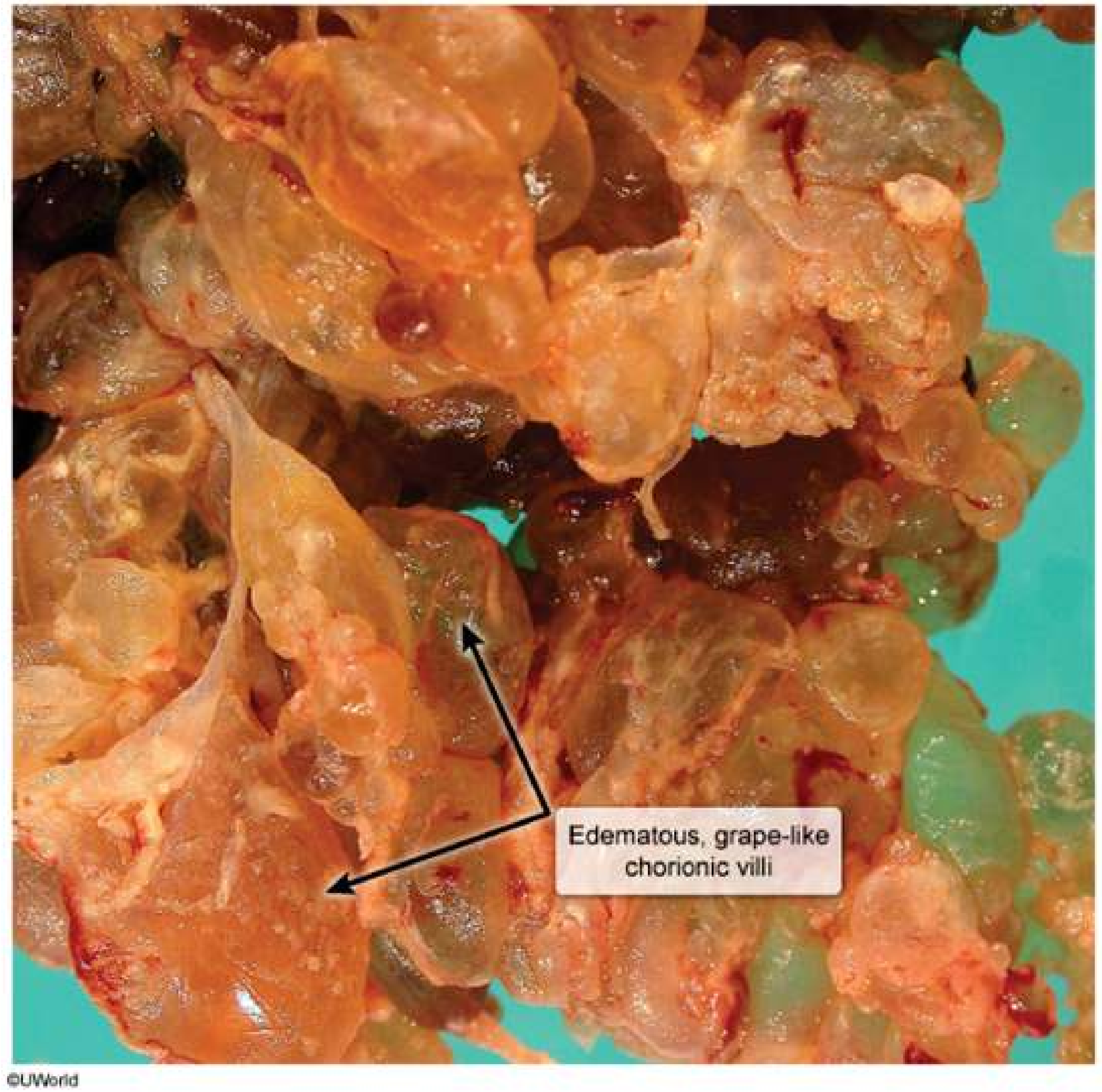
Complete hydatidiform mole


Edematous, grape-like chorionic villi
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The pathology of adenomyosis correlates with its clinical symptoms. Adenomyosis has a gross appearance as

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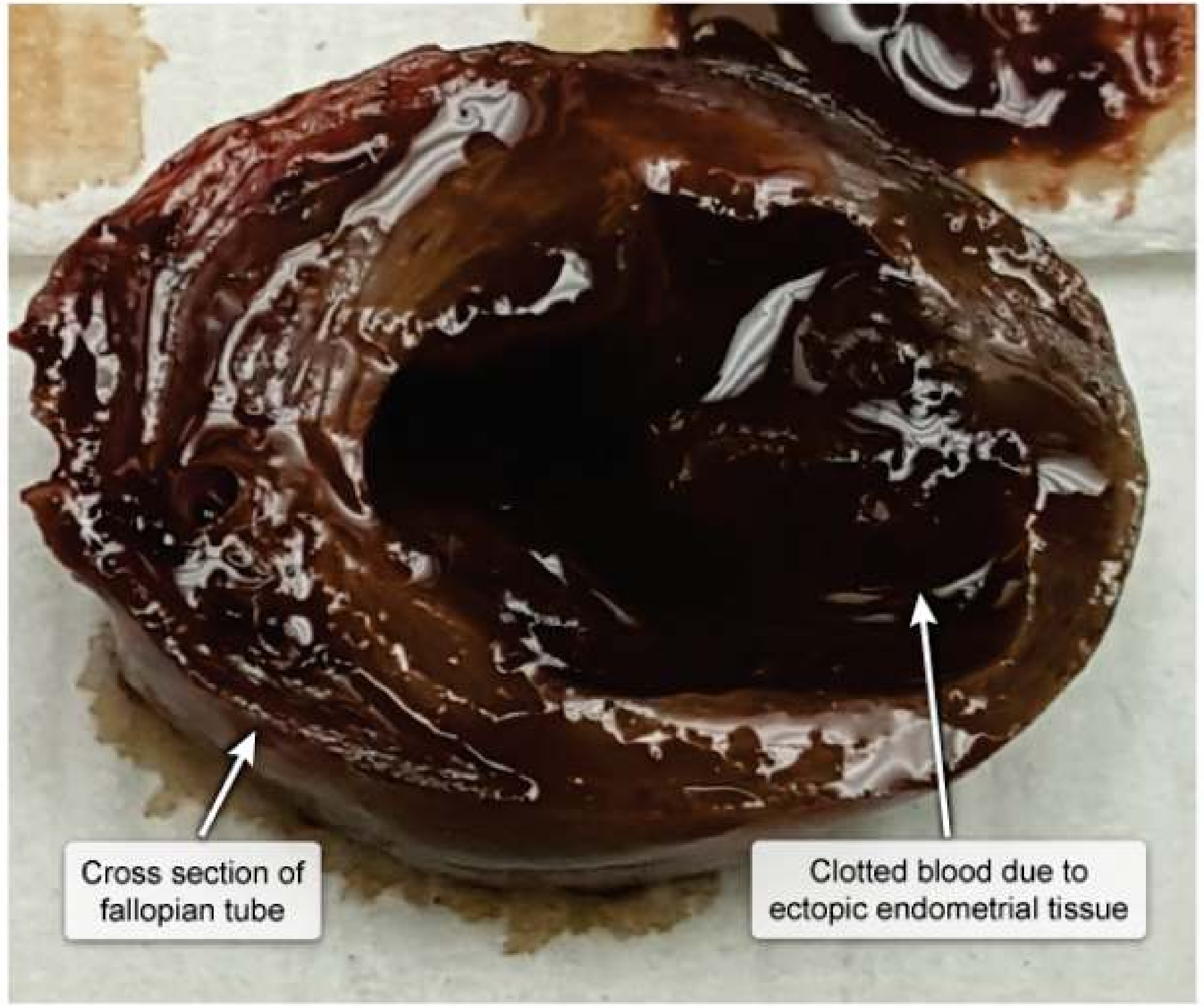
Endometriosis


Cross section of fallopian tube
Clotted blood due to ectopic endometrial tissue

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(Choice F) Uterine sarcomas are malignant uterine tumors. Affected patients typically have irregular,

postmenopausal bleeding rather than regular, heavy menses. Gross pathology typically reveals a discrete uterine

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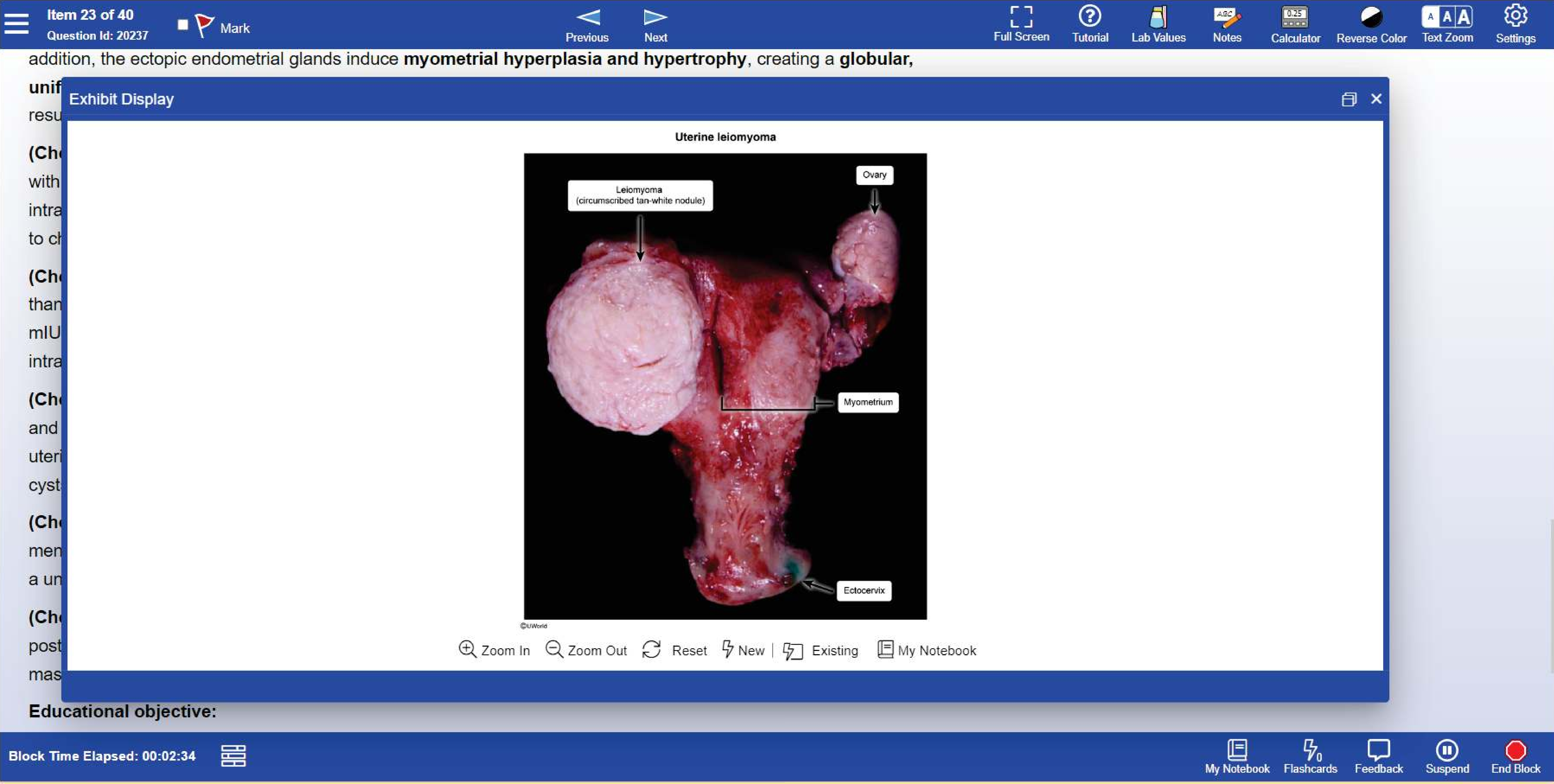
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Leiomyoma
(circumscribed tan-white nodule)
Ovary
Myometrium
Ectocervix
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addition, the ectopic endometrial glands induce **myometrial hyperplasia and hypertrophy**, creating a **globular,**

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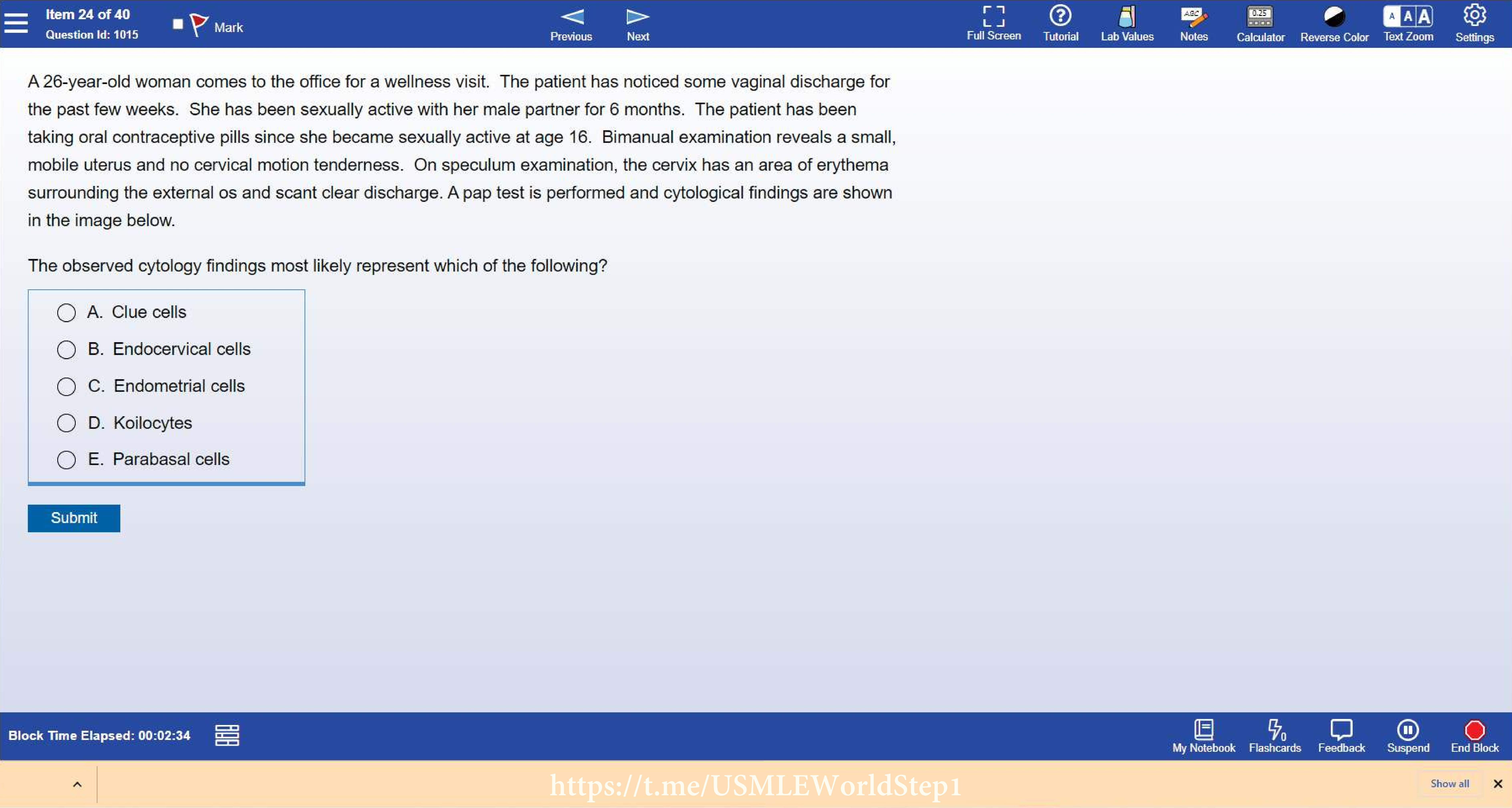
Uterine leiomyoma

Educational objective: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A 26-year-old woman comes to the office for a wellness visit. The patient has noticed some vaginal discharge for the past few weeks. She has been sexually active with her male partner for 6 months. The patient has been taking oral contraceptive pills since she became sexually active at age 16. Bimanual examination reveals a small, mobile uterus and no cervical motion tenderness. On speculum examination, the cervix has an area of erythema surrounding the external os and scant clear discharge. A pap test is performed and cytological findings are shown in the image below.

The observed cytology findings most likely represent which of the following?

- ○ A. Clue cells
- ○ B. Endocervical cells
- ○ C. Endometrial cells
- ○ D. Koilocytes
- ○ E. Parabasal cells

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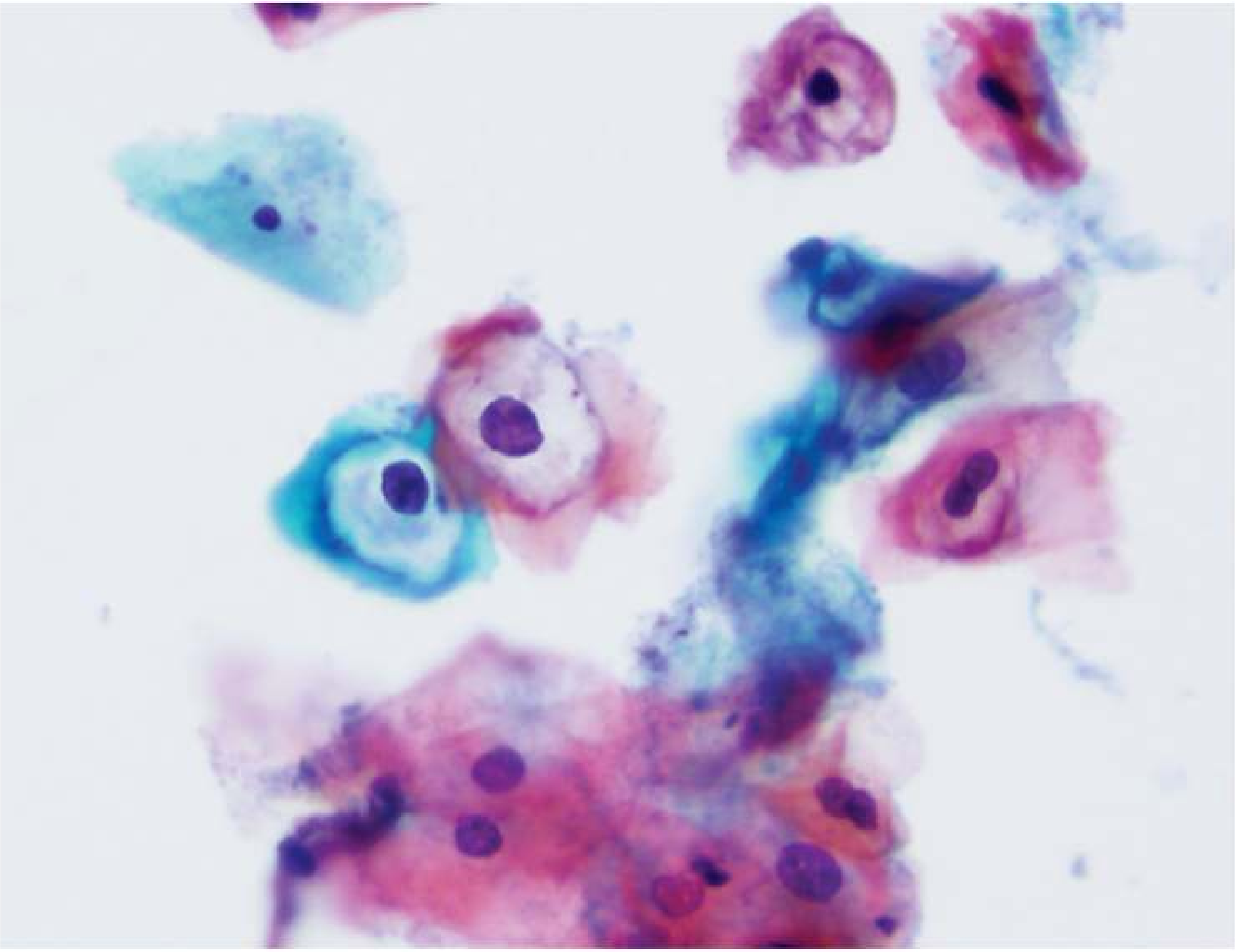

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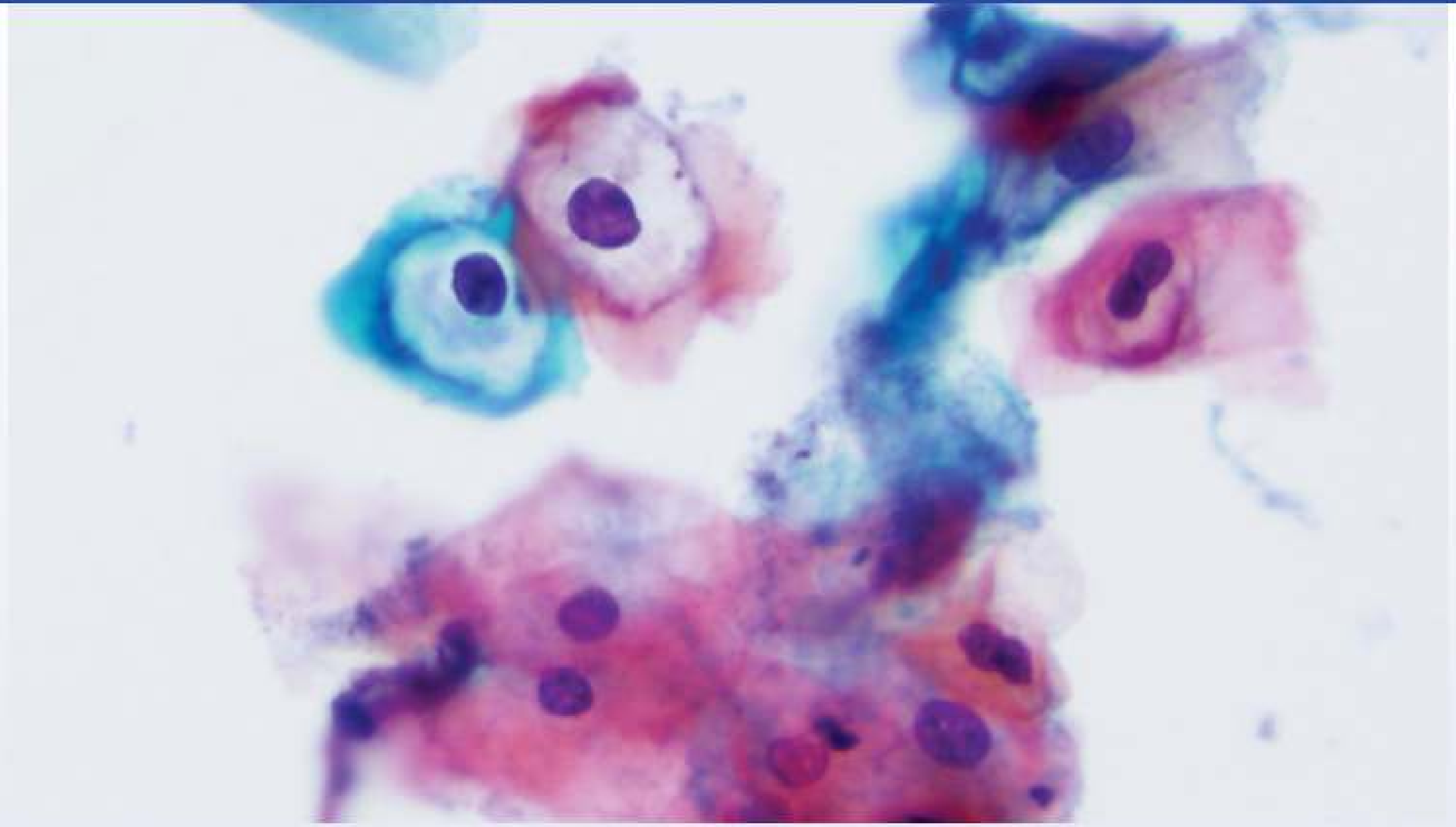

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○ B. Endocervical cells
○ C. Endometrial cells
○ D. Koilocytes
○ E. Parabasal cells

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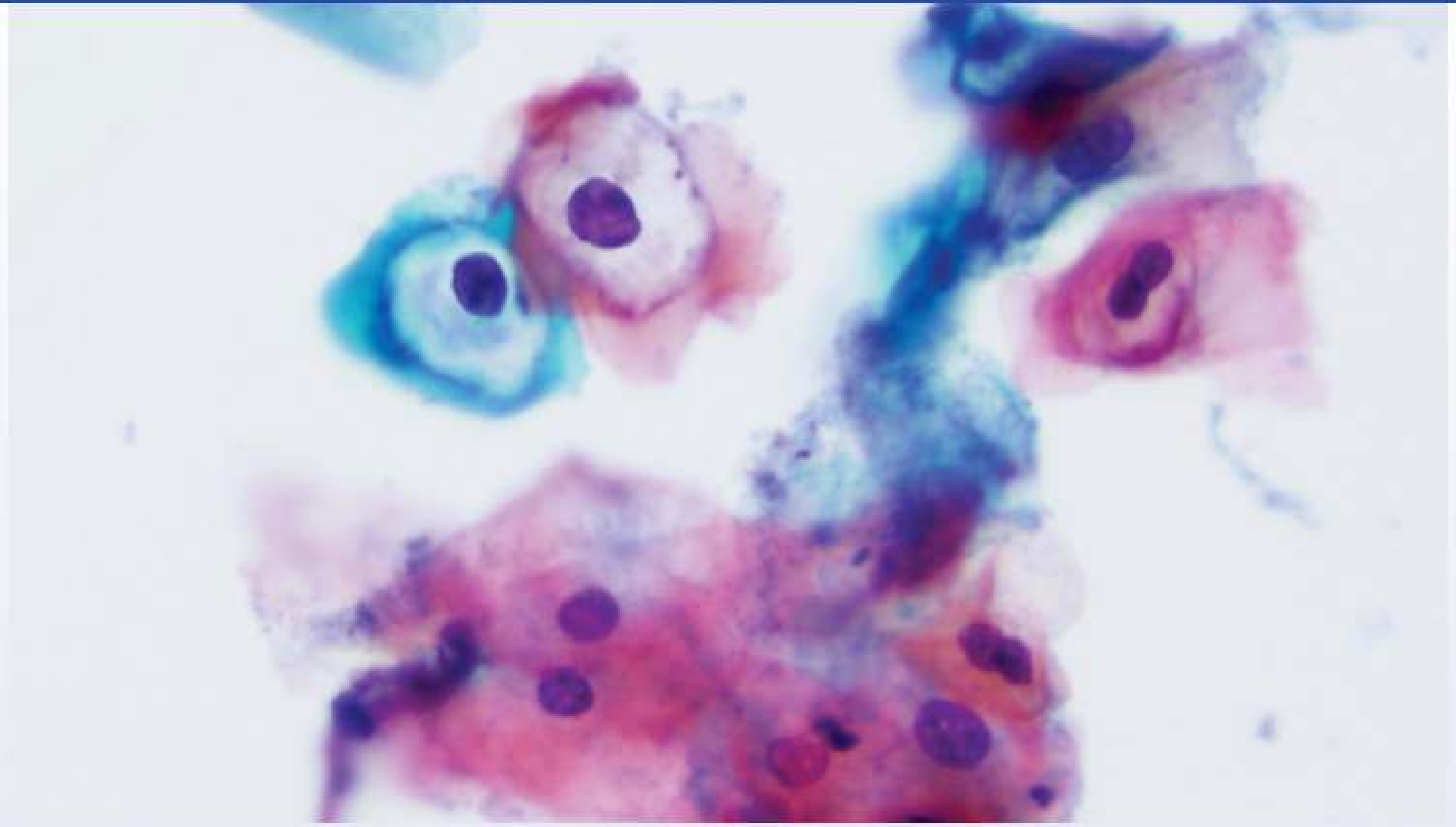

The observed cytology findings most likely represent which of the following?

- ✗ ● A. Clue cells
- ○ B. Endocervical cells
- ○ C. Endometrial cells
- ✓ ○ D. Koilocytes
- ○ E. Parabasal cells

Incorrect
Correct answer
D

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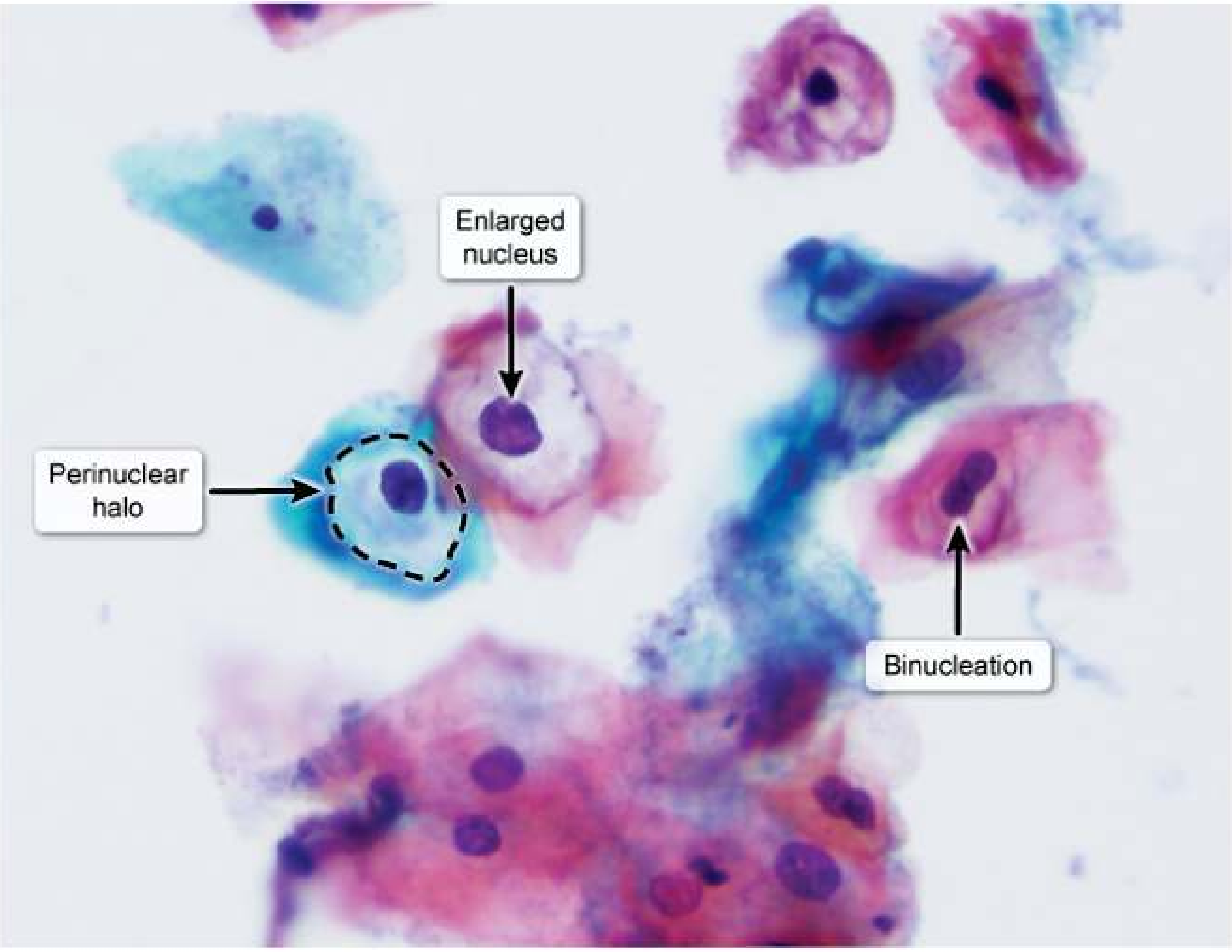
Koilocytes


Enlarged nucleus
Perinuclear halo
Binucleation

Cervical Pap test

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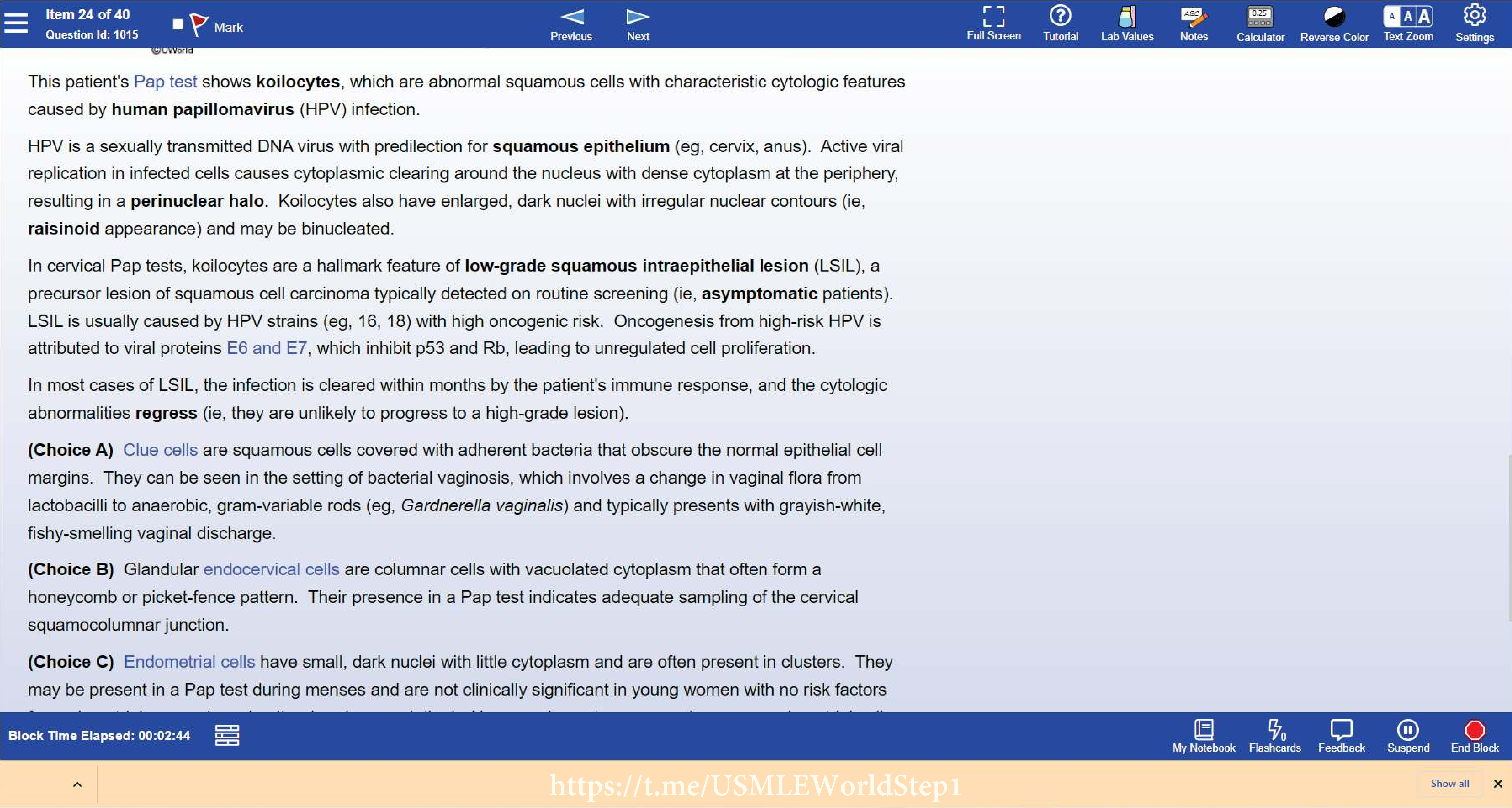
This patient's Pap test shows **koilocytes**, which are abnormal squamous cells with characteristic cytologic features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This patient's Pap test shows **koilocytes**, which are abnormal squamous cells with characteristic cytologic features caused by **human papillomavirus** (HPV) infection.

HPV is a sexually transmitted DNA virus with predilection for **squamous epithelium** (eg, cervix, anus). Active viral replication in infected cells causes cytoplasmic clearing around the nucleus with dense cytoplasm at the periphery, resulting in a **perinuclear halo**. Koilocytes also have enlarged, dark nuclei with irregular nuclear contours (ie, **raisinoid** appearance) and may be binucleated.

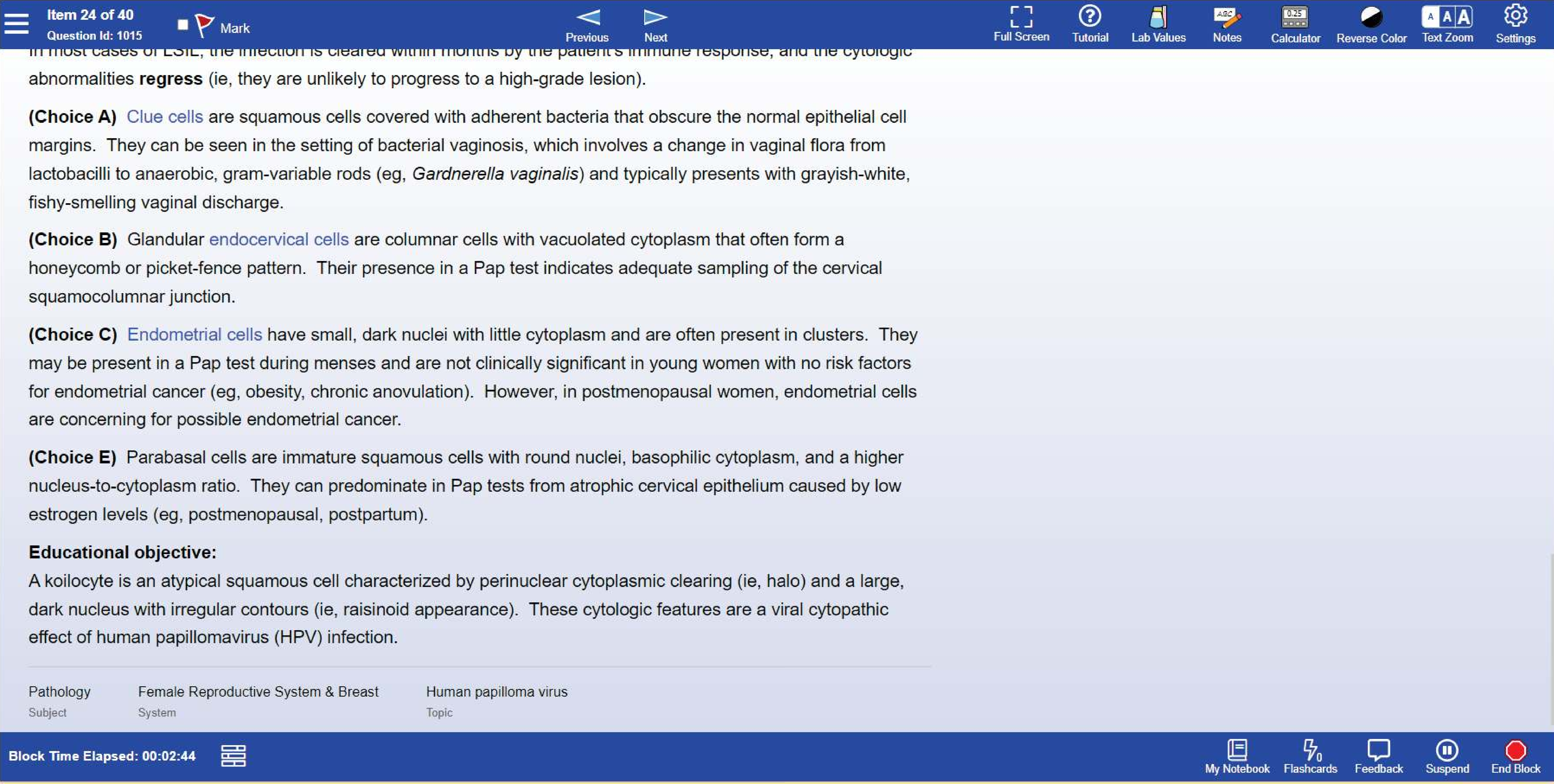
In cervical Pap tests, koilocytes are a hallmark feature of **low-grade squamous intraepithelial lesion** (LSIL), a precursor lesion of squamous cell carcinoma typically detected on routine screening (ie, **asymptomatic** patients). LSIL is usually caused by HPV strains (eg, 16, 18) with high oncogenic risk. Oncogenesis from high-risk HPV is attributed to viral proteins E6 and E7, which inhibit p53 and Rb, leading to unregulated cell proliferation.

In most cases of LSIL, the infection is cleared within months by the patient's immune response, and the cytologic abnormalities **regress** (ie, they are unlikely to progress to a high-grade lesion).

(Choice A) Clue cells are squamous cells covered with adherent bacteria that obscure the normal epithelial cell margins. They can be seen in the setting of bacterial vaginosis, which involves a change in vaginal flora from lactobacilli to anaerobic, gram-variable rods (eg, *Gardnerella vaginalis*) and typically presents with grayish-white, fishy-smelling vaginal discharge.

(Choice B) Glandular endocervical cells are columnar cells with vacuolated cytoplasm that often form a honeycomb or picket-fence pattern. Their presence in a Pap test indicates adequate sampling of the cervical squamocolumnar junction.

(Choice C) Endometrial cells have small, dark nuclei with little cytoplasm and are often present in clusters. They may be present in a Pap test during menses and are not clinically significant in young women with no risk factors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(Choice B) Glandular endocervical cells are columnar cells with vacuolated cytoplasm that often form a honeycomb or picket-fence pattern. Their presence in a Pap test indicates adequate sampling of the cervical squamocolumnar junction.

(Choice C) Endometrial cells have small, dark nuclei with little cytoplasm and are often present in clusters. They may be present in a Pap test during menses and are not clinically significant in young women with no risk factors for endometrial cancer (eg, obesity, chronic anovulation). However, in postmenopausal women, endometrial cells are concerning for possible endometrial cancer.

(Choice E) Parabasal cells are immature squamous cells with round nuclei, basophilic cytoplasm, and a higher nucleus-to-cytoplasm ratio. They can predominate in Pap tests from atrophic cervical epithelium caused by low estrogen levels (eg, postmenopausal, postpartum).

Educational objective:
A koilocyte is an atypical squamous cell characterized by perinuclear cytoplasmic clearing (ie, halo) and a large, dark nucleus with irregular contours (ie, raisinoid appearance). These cytologic features are a viral cytopathic effect of human papillomavirus (HPV) infection.

Pathology	Female Reproductive System & Breast	Human papilloma virus
Subject	System	Topic

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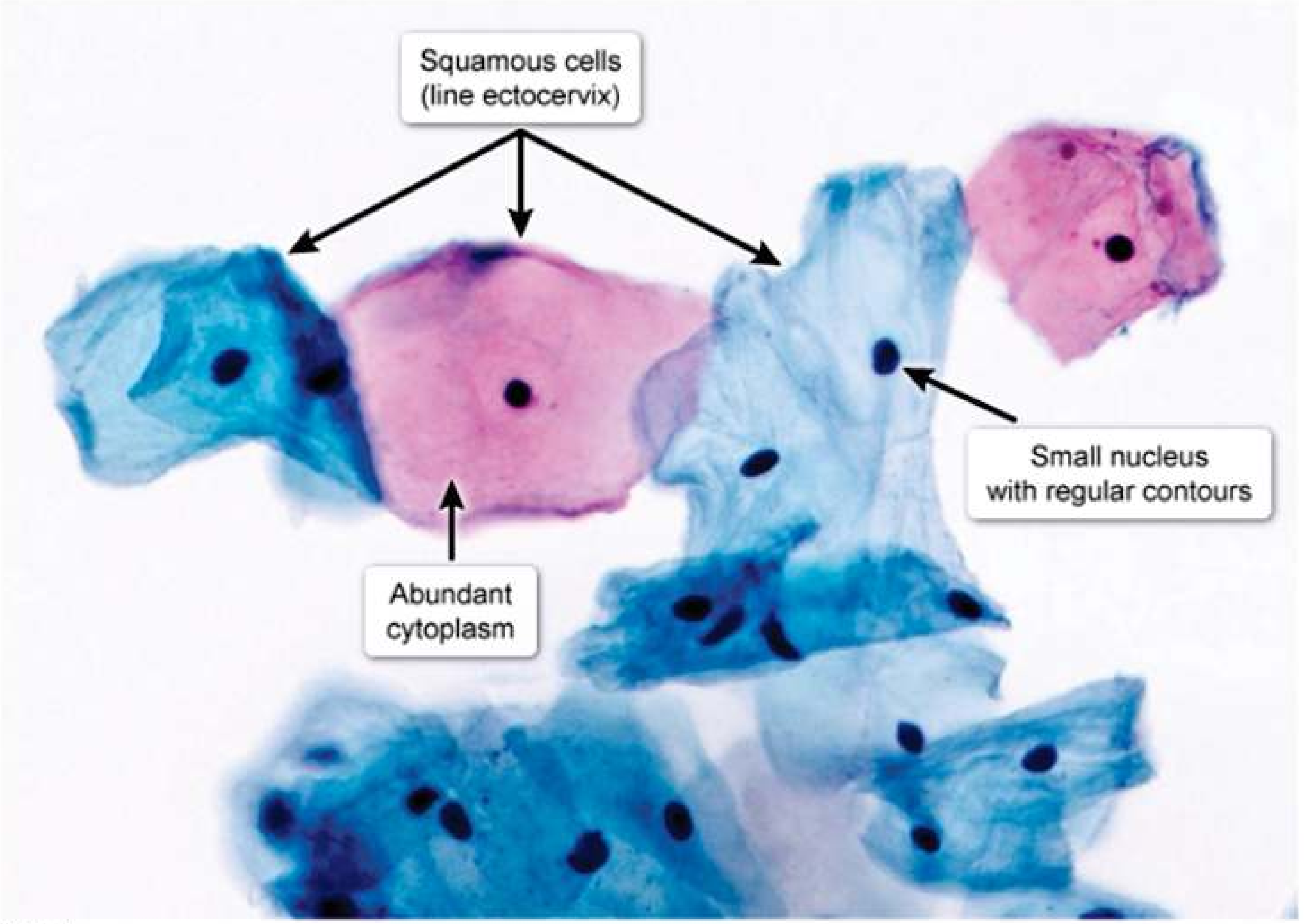
Binucleation

Exhibit Display

Normal cervical Pap test


Squamous cells (line ectocervix)
Small nucleus with regular contours
Abundant cytoplasm

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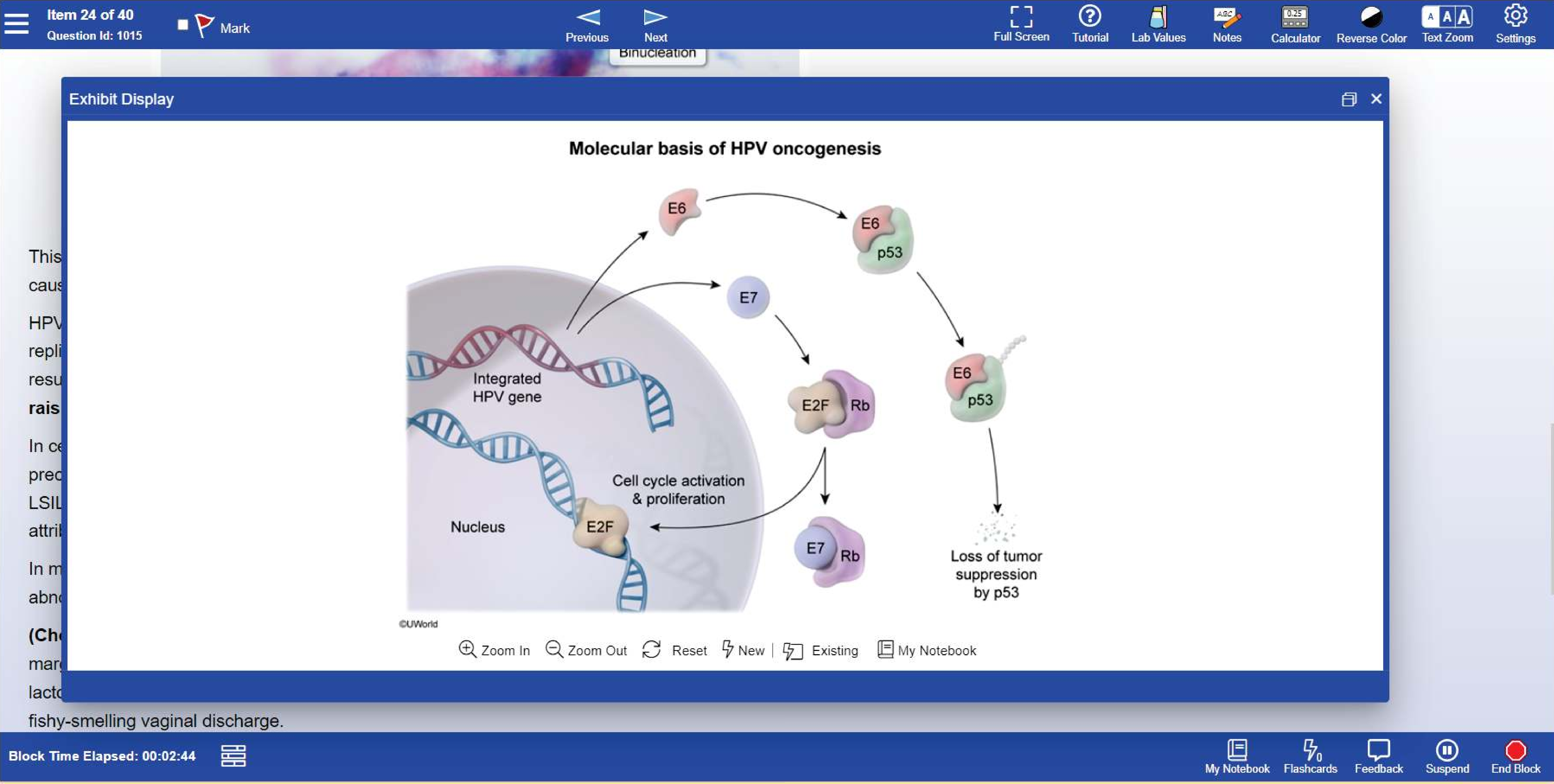
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Binucleation
Exhibit Display

Molecular basis of HPV oncogenesis

E6
E6
p53
E7
E2F
Rb
E6
p53
Integrated
HPV gene
Cell cycle activation
& proliferation
Nucleus
E2F
E7
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Loss of tumor
suppression
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may be present in a Pap test during menses and are not clinically significant in young women with no risk factors

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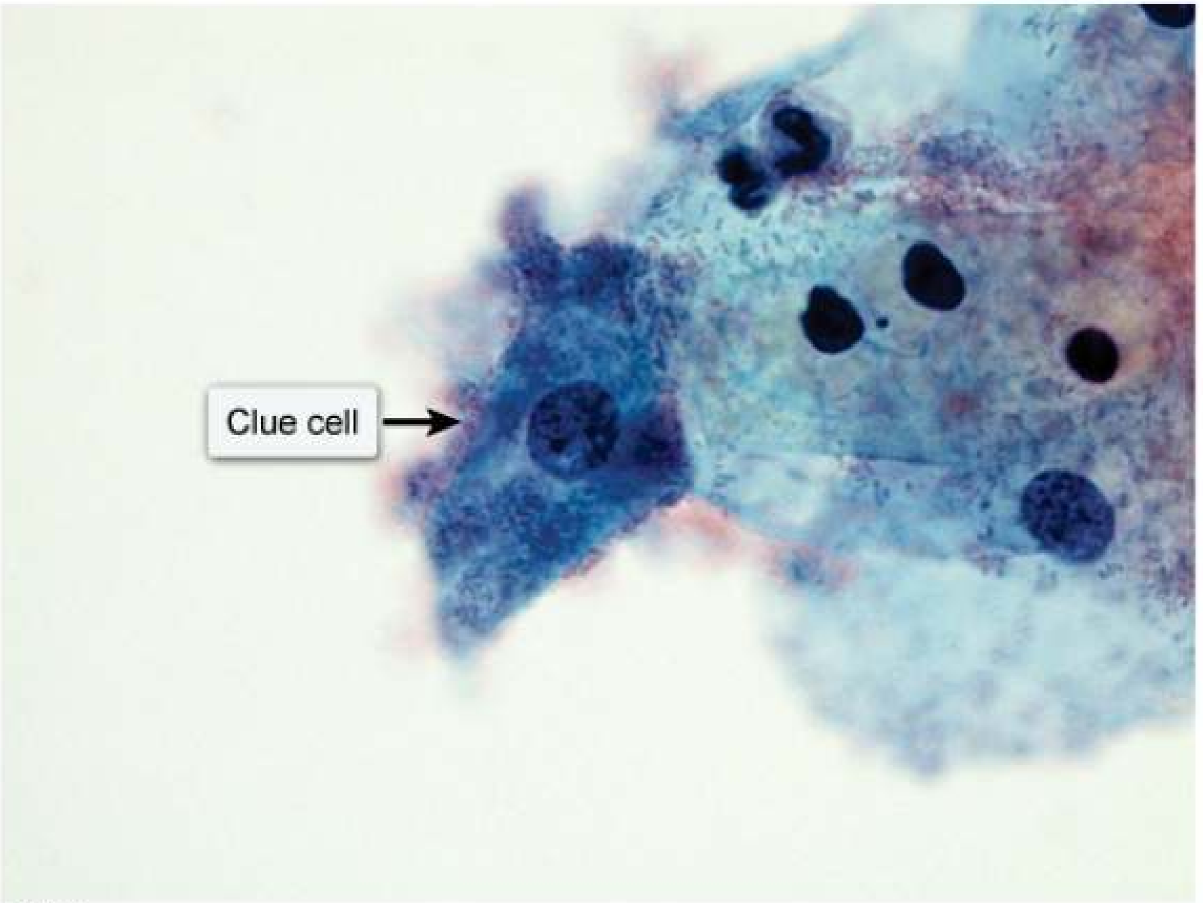
Bacterial vaginosis



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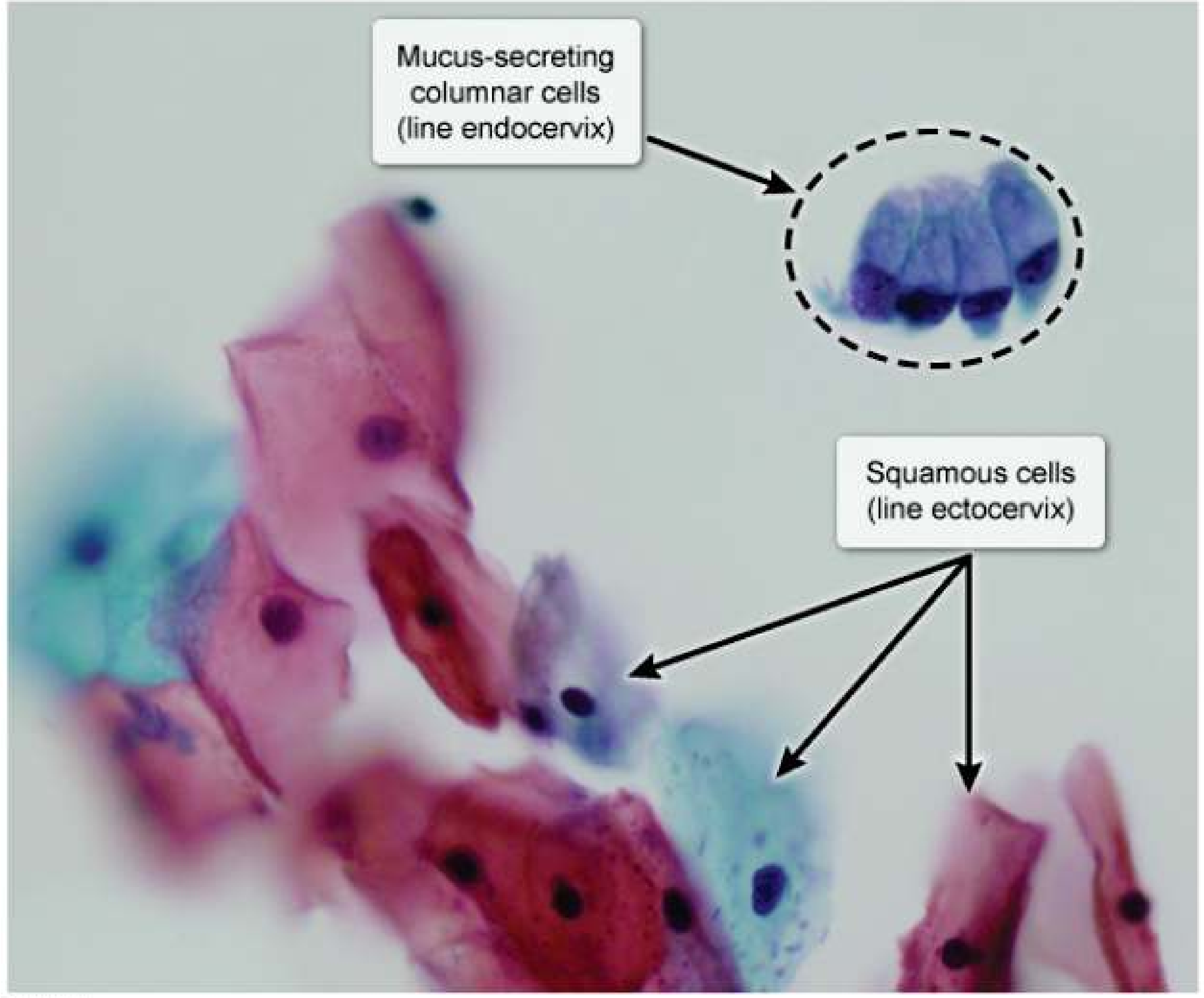
Normal cervical Pap test


Mucus-secreting columnar cells (line endocervix)
Squamous cells (line ectocervix)

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may be present in a Pap test during menses and are not clinically significant in young women with no risk factors

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LSIL is usually caused by HPV strains (eg, 16, 18) with high oncogenic risk. Oncogenesis from high-risk HPV is attri

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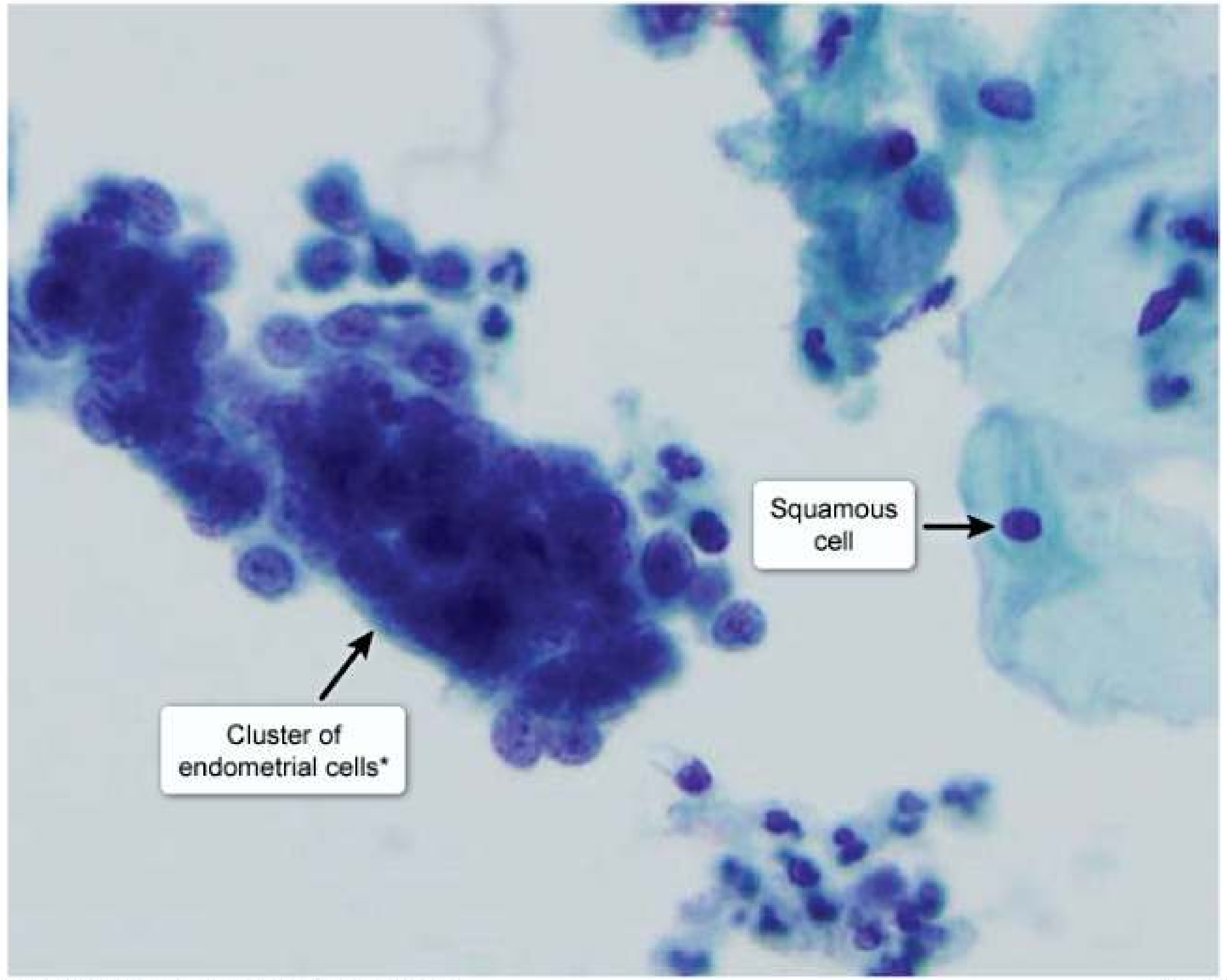
Endometrial cells


Squamous cell
Cluster of endometrial cells*

*Small cells with dark nuclei and little cytoplasm.

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effect of human papillomavirus (HPV) infection.

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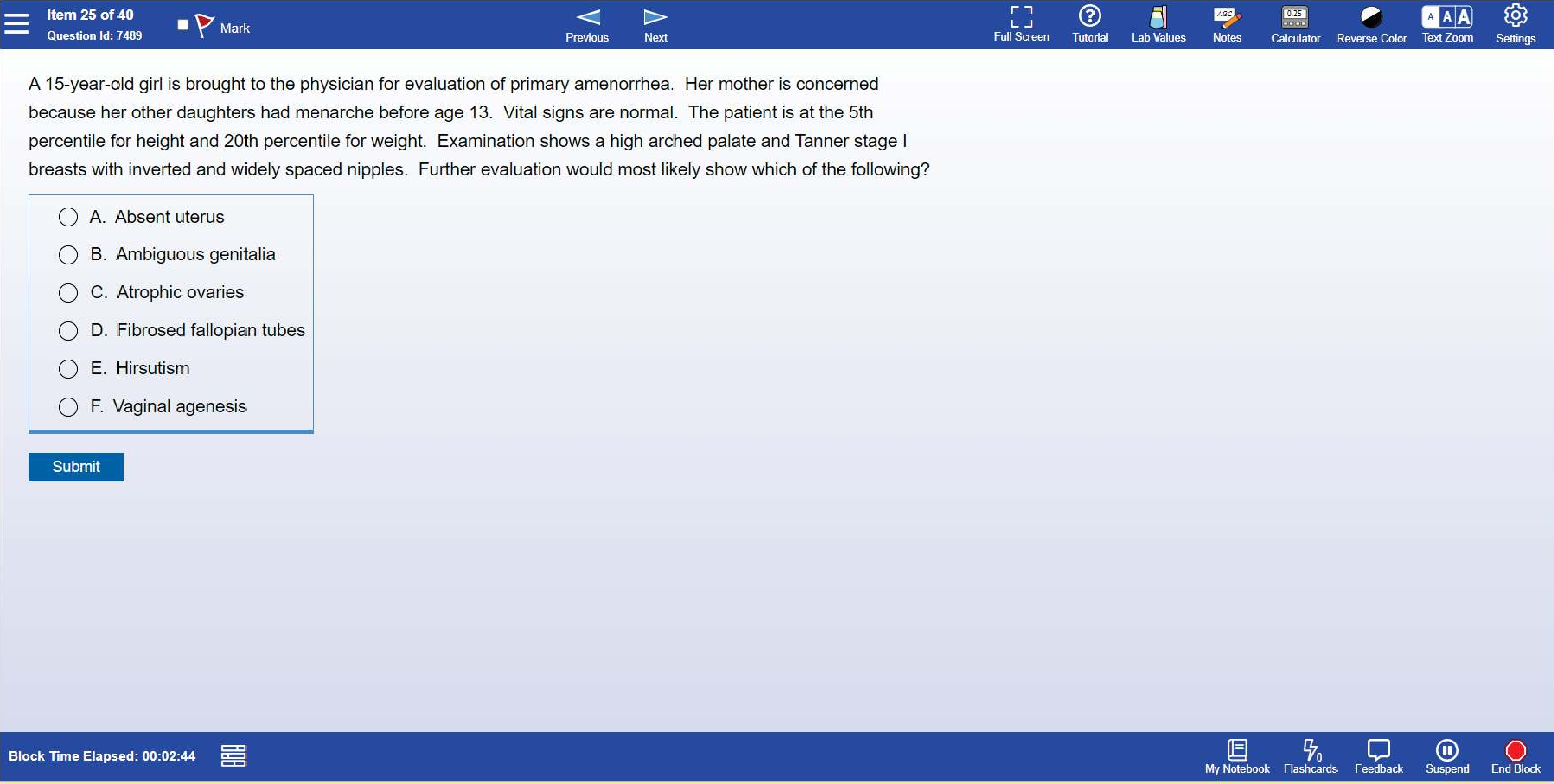
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A 15-year-old girl is brought to the physician for evaluation of primary amenorrhea. Her mother is concerned because her other daughters had menarche before age 13. Vital signs are normal. The patient is at the 5th percentile for height and 20th percentile for weight. Examination shows a high arched palate and Tanner stage I breasts with inverted and widely spaced nipples. Further evaluation would most likely show which of the following?

○ A. Absent uterus
○ B. Ambiguous genitalia
○ C. Atrophic ovaries
○ D. Fibrosed fallopian tubes
○ E. Hirsutism
○ F. Vaginal agenesis

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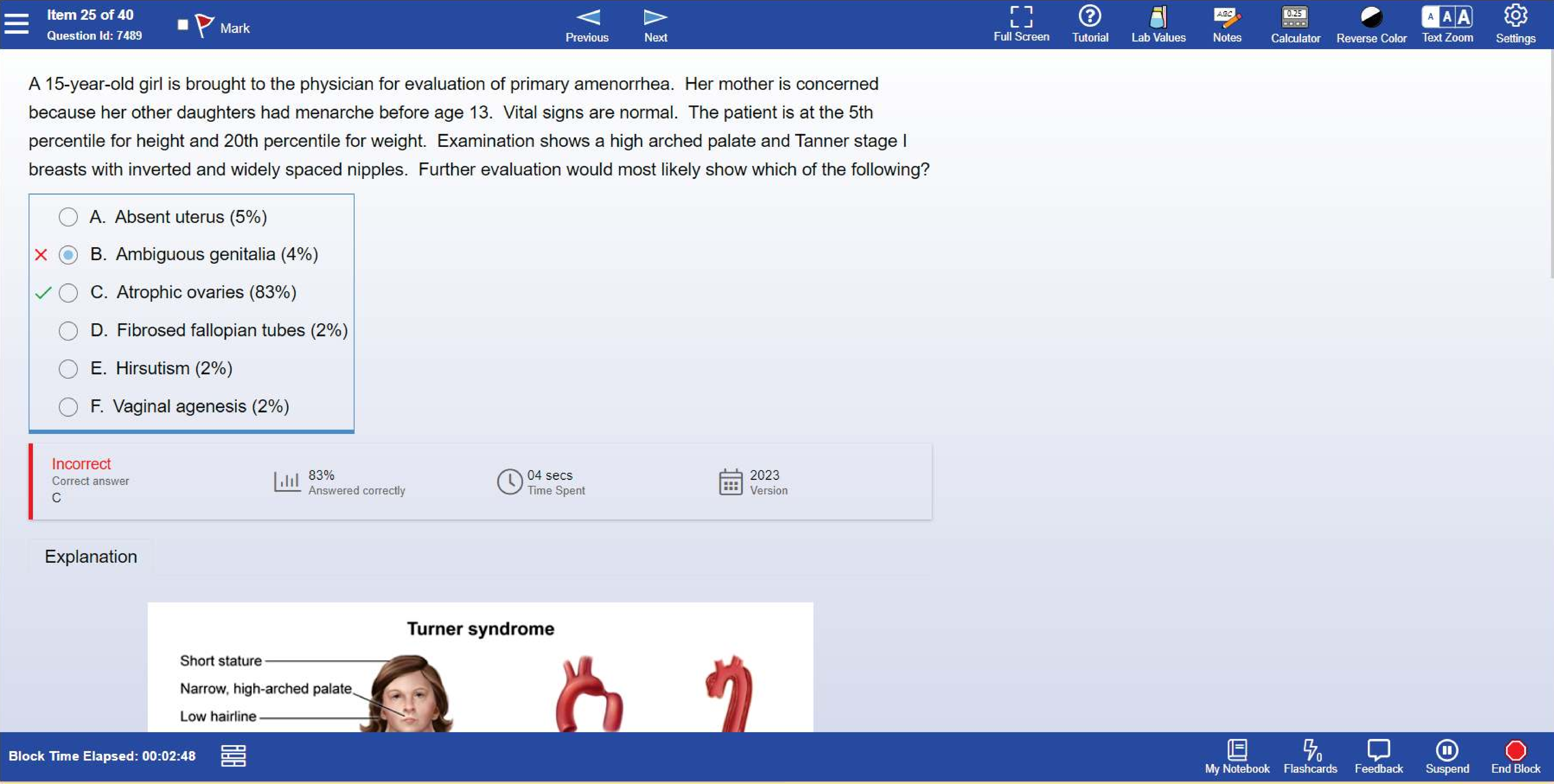
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A 15-year-old girl is brought to the physician for evaluation of primary amenorrhea. Her mother is concerned because her other daughters had menarche before age 13. Vital signs are normal. The patient is at the 5th percentile for height and 20th percentile for weight. Examination shows a high arched palate and Tanner stage I breasts with inverted and widely spaced nipples. Further evaluation would most likely show which of the following?

- ○ A. Absent uterus (5%)
- ✗ ● B. Ambiguous genitalia (4%)
- ✓ ○ C. Atrophic ovaries (83%)
- ○ D. Fibrosed fallopian tubes (2%)
- ○ E. Hirsutism (2%)
- ○ F. Vaginal agenesis (2%)

Incorrect
Correct answer
C

83%
Answered correctly

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Explanation

Turner syndrome

Short stature
Narrow, high-arched palate
Low hairline

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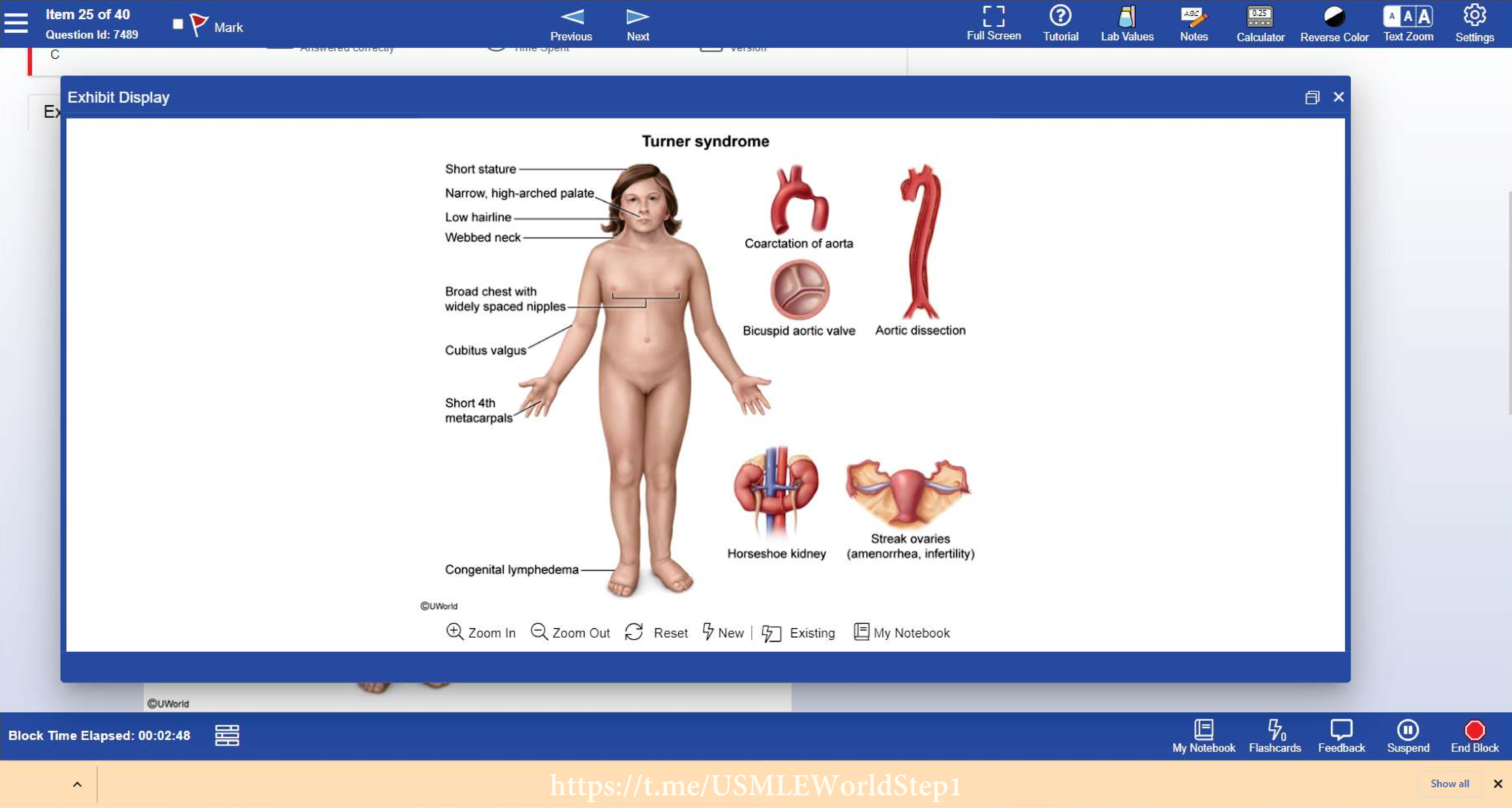
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Turner syndrome
Short stature
Narrow, high-arched palate
Low hairline
Webbed neck
Broad chest with widely spaced nipples
Cubitus valgus
Short 4th metacarpals
Congenital lymphedema
Coarctation of aorta
Bicuspid aortic valve
Aortic dissection
Horseshoe kidney
Streak ovaries (amenorrhea, infertility)
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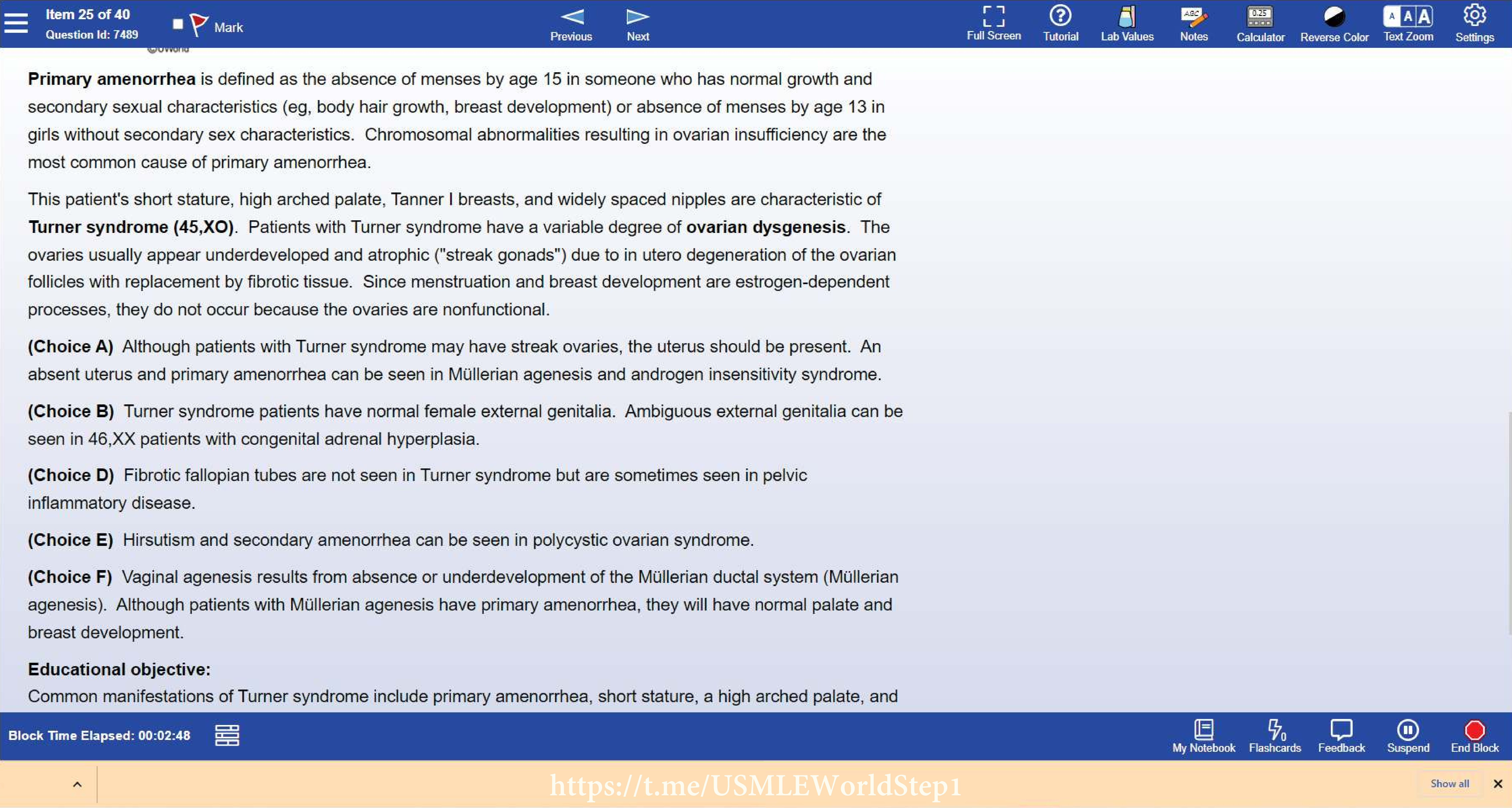
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Primary amenorrhea is defined as the absence of menses by age 15 in someone who has normal growth and secondary sexual characteristics (eg, body hair growth, breast development) or absence of menses by age 13 in girls without secondary sex characteristics. Chromosomal abnormalities resulting in ovarian insufficiency are the most common cause of primary amenorrhea.

This patient's short stature, high arched palate, Tanner I breasts, and widely spaced nipples are characteristic of **Turner syndrome (45,XO)**. Patients with Turner syndrome have a variable degree of **ovarian dysgenesis**. The ovaries usually appear underdeveloped and atrophic ("streak gonads") due to in utero degeneration of the ovarian follicles with replacement by fibrotic tissue. Since menstruation and breast development are estrogen-dependent processes, they do not occur because the ovaries are nonfunctional.

(Choice A) Although patients with Turner syndrome may have streak ovaries, the uterus should be present. An absent uterus and primary amenorrhea can be seen in Müllerian agenesis and androgen insensitivity syndrome.

(Choice B) Turner syndrome patients have normal female external genitalia. Ambiguous external genitalia can be seen in 46,XX patients with congenital adrenal hyperplasia.

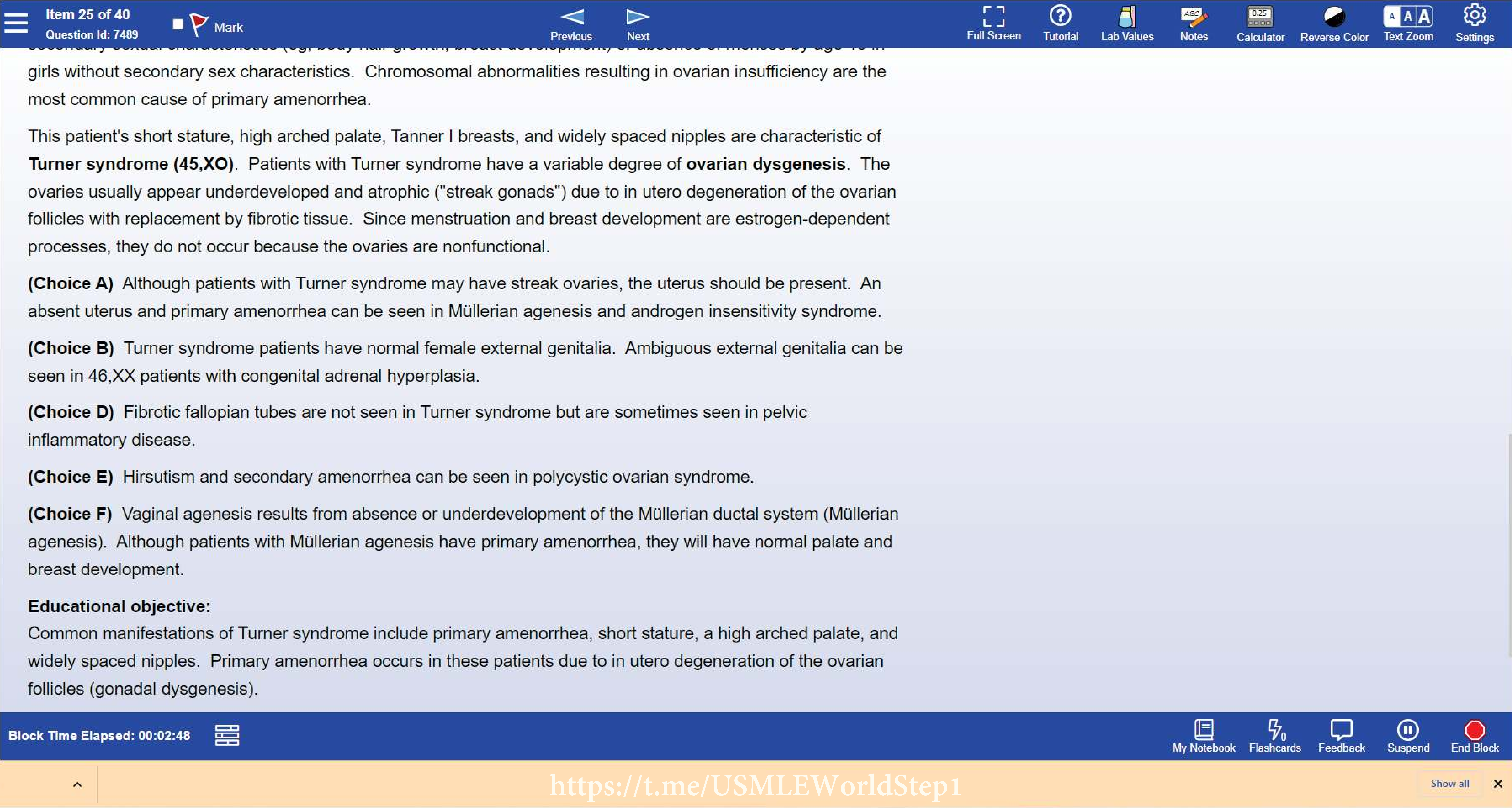
(Choice D) Fibrotic fallopian tubes are not seen in Turner syndrome but are sometimes seen in pelvic inflammatory disease.

(Choice E) Hirsutism and secondary amenorrhea can be seen in polycystic ovarian syndrome.

(Choice F) Vaginal agenesis results from absence or underdevelopment of the Müllerian ductal system (Müllerian agenesis). Although patients with Müllerian agenesis have primary amenorrhea, they will have normal palate and breast development.

Educational objective:

Common manifestations of Turner syndrome include primary amenorrhea, short stature, a high arched palate, and



girls without secondary sex characteristics. Chromosomal abnormalities resulting in ovarian insufficiency are the most common cause of primary amenorrhea.

This patient's short stature, high arched palate, Tanner I breasts, and widely spaced nipples are characteristic of **Turner syndrome (45,XO)**. Patients with Turner syndrome have a variable degree of **ovarian dysgenesis**. The ovaries usually appear underdeveloped and atrophic ("streak gonads") due to in utero degeneration of the ovarian follicles with replacement by fibrotic tissue. Since menstruation and breast development are estrogen-dependent processes, they do not occur because the ovaries are nonfunctional.

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Educational objective:

Common manifestations of Turner syndrome include primary amenorrhea, short stature, a high arched palate, and widely spaced nipples. Primary amenorrhea occurs in these patients due to in utero degeneration of the ovarian follicles (gonadal dysgenesis).

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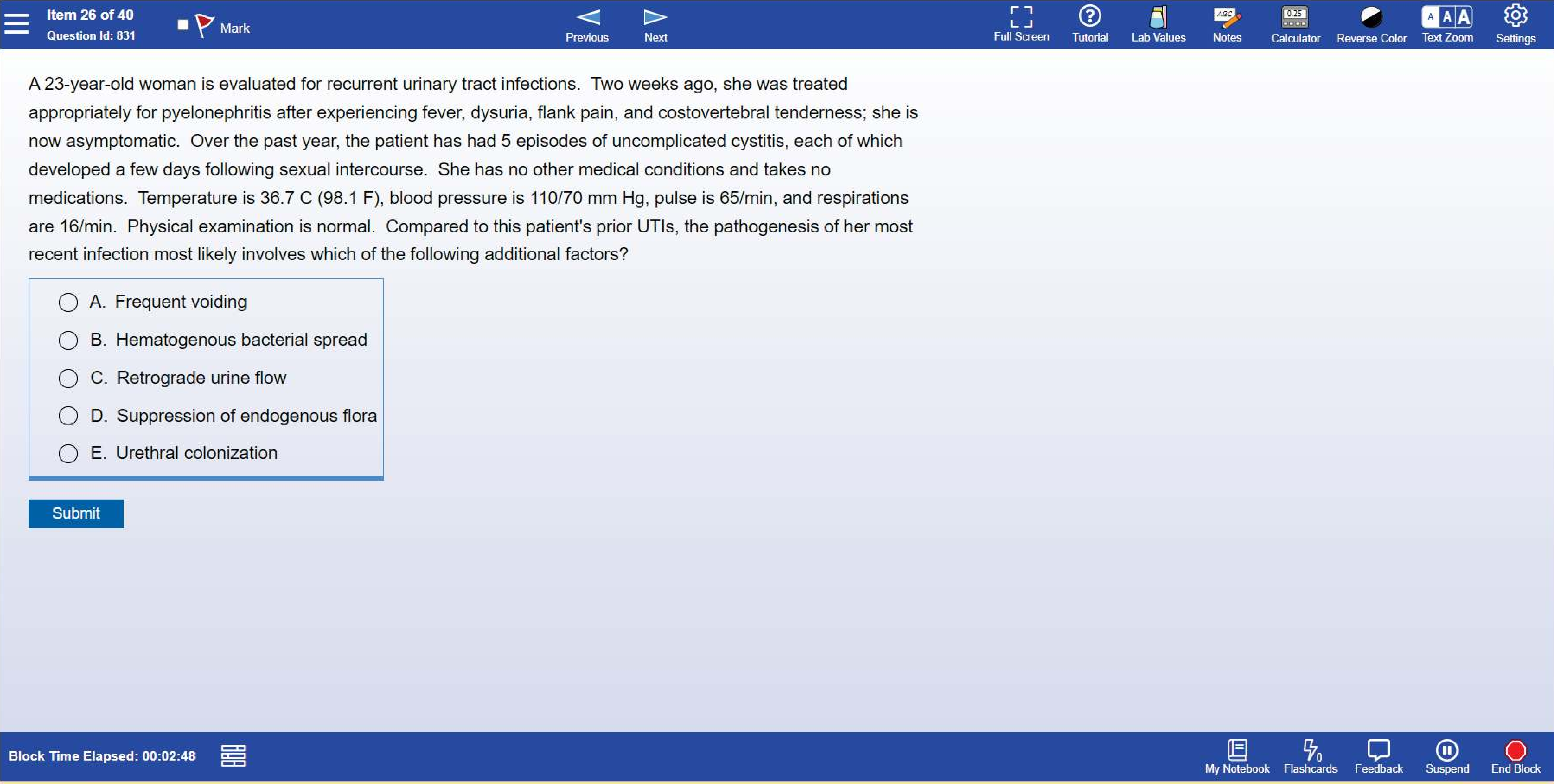
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A 23-year-old woman is evaluated for recurrent urinary tract infections. Two weeks ago, she was treated appropriately for pyelonephritis after experiencing fever, dysuria, flank pain, and costovertebral tenderness; she is now asymptomatic. Over the past year, the patient has had 5 episodes of uncomplicated cystitis, each of which developed a few days following sexual intercourse. She has no other medical conditions and takes no medications. Temperature is 36.7 C (98.1 F), blood pressure is 110/70 mm Hg, pulse is 65/min, and respirations are 16/min. Physical examination is normal. Compared to this patient's prior UTIs, the pathogenesis of her most recent infection most likely involves which of the following additional factors?

- ○ A. Frequent voiding
- ○ B. Hematogenous bacterial spread
- ○ C. Retrograde urine flow
- ○ D. Suppression of endogenous flora
- ○ E. Urethral colonization

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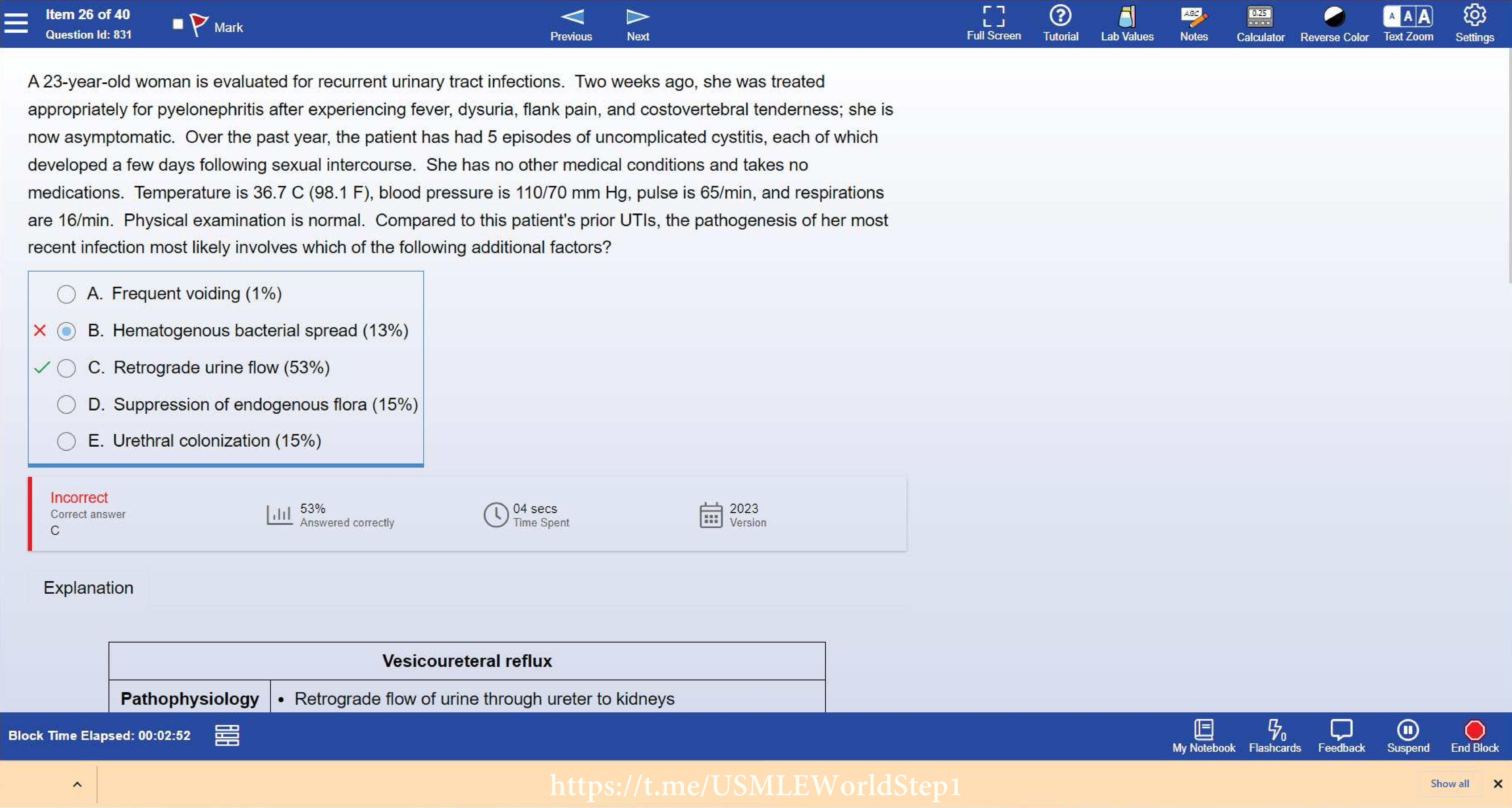
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○ A. Frequent voiding (1%)

✗ ● B. Hematogenous bacterial spread (13%)

✓ ○ C. Retrograde urine flow (53%)

○ D. Suppression of endogenous flora (15%)

○ E. Urethral colonization (15%)

Incorrect
Correct answer
C

53%
Answered correctly

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Explanation

Vesicoureteral reflux	
Pathophysiology	• Retrograde flow of urine through ureter to kidneys

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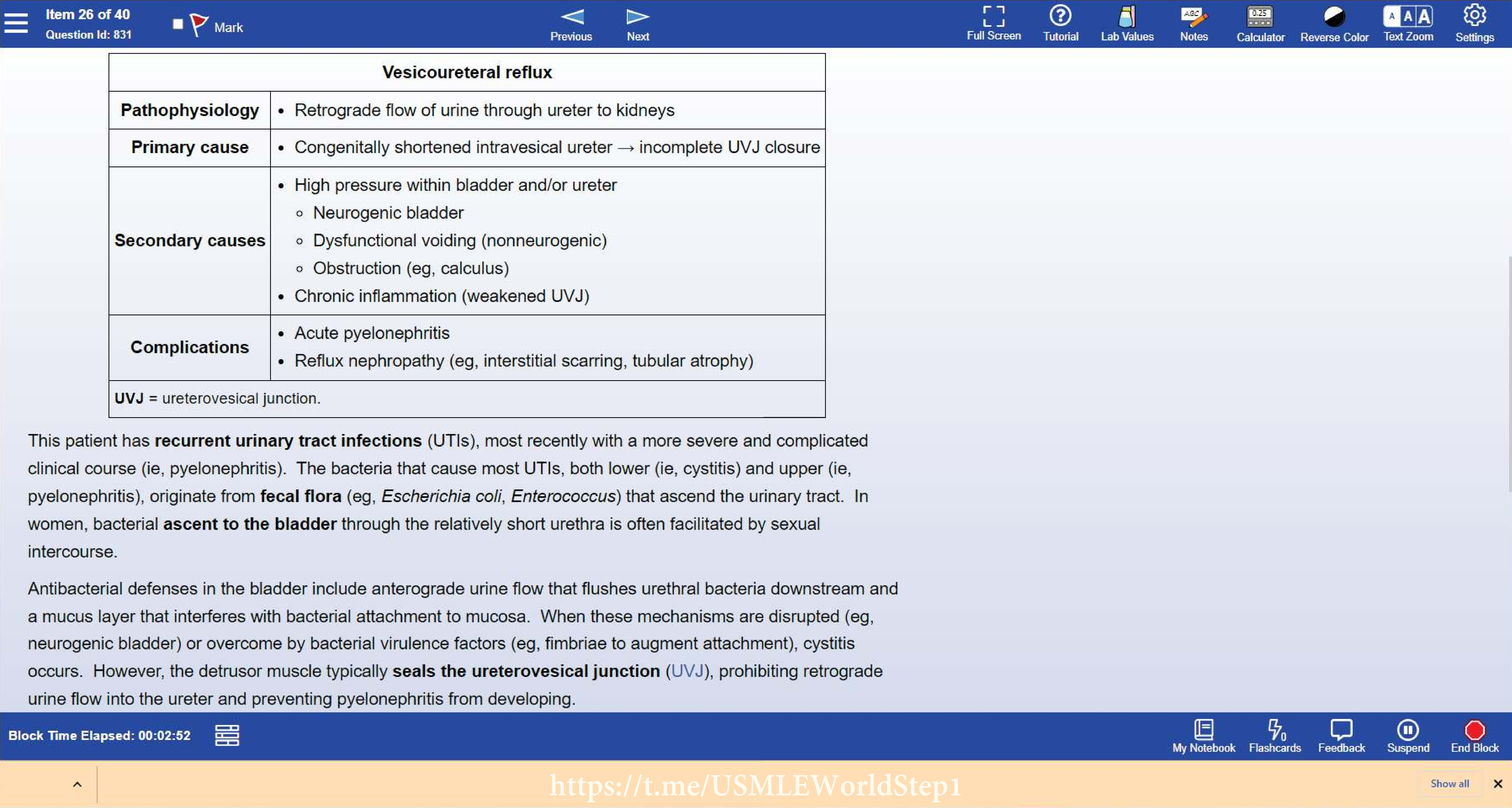
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Vesicoureteral reflux	
Pathophysiology	• Retrograde flow of urine through ureter to kidneys
Primary cause	• Congenitally shortened intravesical ureter → incomplete UVJ closure
Secondary causes	• High pressure within bladder and/or ureter ∘ Neurogenic bladder ∘ Dysfunctional voiding (nonneurogenic) ∘ Obstruction (eg, calculus) • Chronic inflammation (weakened UVJ)
Complications	• Acute pyelonephritis • Reflux nephropathy (eg, interstitial scarring, tubular atrophy)
UVJ = ureterovesical junction.	

This patient has **recurrent urinary tract infections** (UTIs), most recently with a more severe and complicated clinical course (ie, pyelonephritis). The bacteria that cause most UTIs, both lower (ie, cystitis) and upper (ie, pyelonephritis), originate from **fecal flora** (eg, *Escherichia coli*, *Enterococcus*) that ascend the urinary tract. In women, bacterial **ascent to the bladder** through the relatively short urethra is often facilitated by sexual intercourse.

Antibacterial defenses in the bladder include anterograde urine flow that flushes urethral bacteria downstream and a mucus layer that interferes with bacterial attachment to mucosa. When these mechanisms are disrupted (eg, neurogenic bladder) or overcome by bacterial virulence factors (eg, fimbriae to augment attachment), cystitis occurs. However, the detrusor muscle typically **seals the ureterovesical junction** (UVJ), prohibiting retrograde urine flow into the ureter and preventing pyelonephritis from developing.

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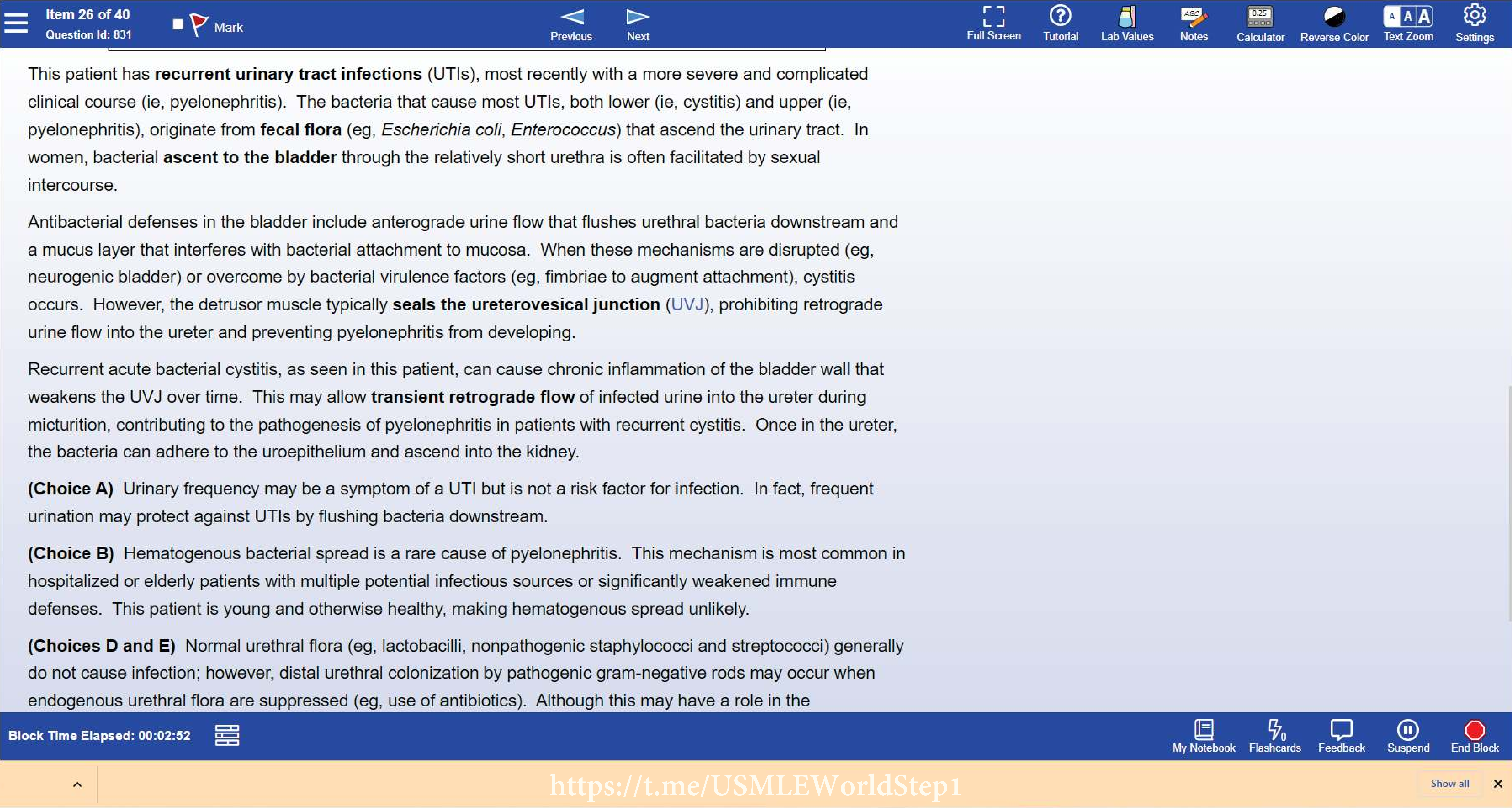

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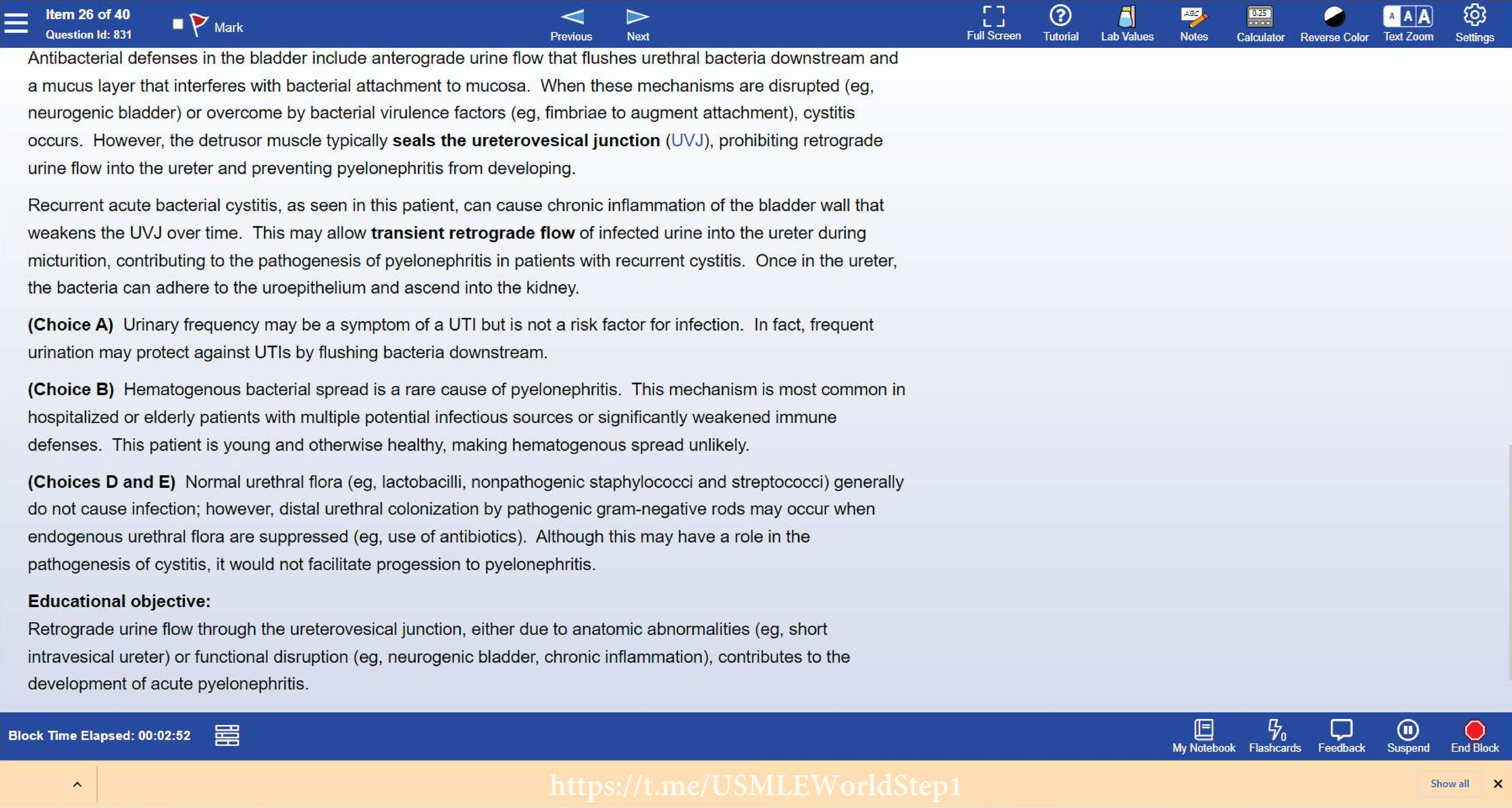
Recurrent acute bacterial cystitis, as seen in this patient, can cause chronic inflammation of the bladder wall that weakens the UVJ over time. This may allow **transient retrograde flow** of infected urine into the ureter during micturition, contributing to the pathogenesis of pyelonephritis in patients with recurrent cystitis. Once in the ureter, the bacteria can adhere to the uroepithelium and ascend into the kidney.

(Choice A) Urinary frequency may be a symptom of a UTI but is not a risk factor for infection. In fact, frequent urination may protect against UTIs by flushing bacteria downstream.

(Choice B) Hematogenous bacterial spread is a rare cause of pyelonephritis. This mechanism is most common in hospitalized or elderly patients with multiple potential infectious sources or significantly weakened immune defenses. This patient is young and otherwise healthy, making hematogenous spread unlikely.

(Choices D and E) Normal urethral flora (eg, lactobacilli, nonpathogenic staphylococci and streptococci) generally do not cause infection; however, distal urethral colonization by pathogenic gram-negative rods may occur when endogenous urethral flora are suppressed (eg, use of antibiotics). Although this may have a role in the



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Educational objective:

Retrograde urine flow through the ureterovesical junction, either due to anatomic abnormalities (eg, short intravesical ureter) or functional disruption (eg, neurogenic bladder, chronic inflammation), contributes to the development of acute pyelonephritis.

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pyelonephritis), originate from **fecal flora** (eg, *Escherichia coli*, *Enterococcus*) that ascend the urinary tract. In wom bacterial ascent to the bladder through the relatively short urethra is often facilitated by sexual inter

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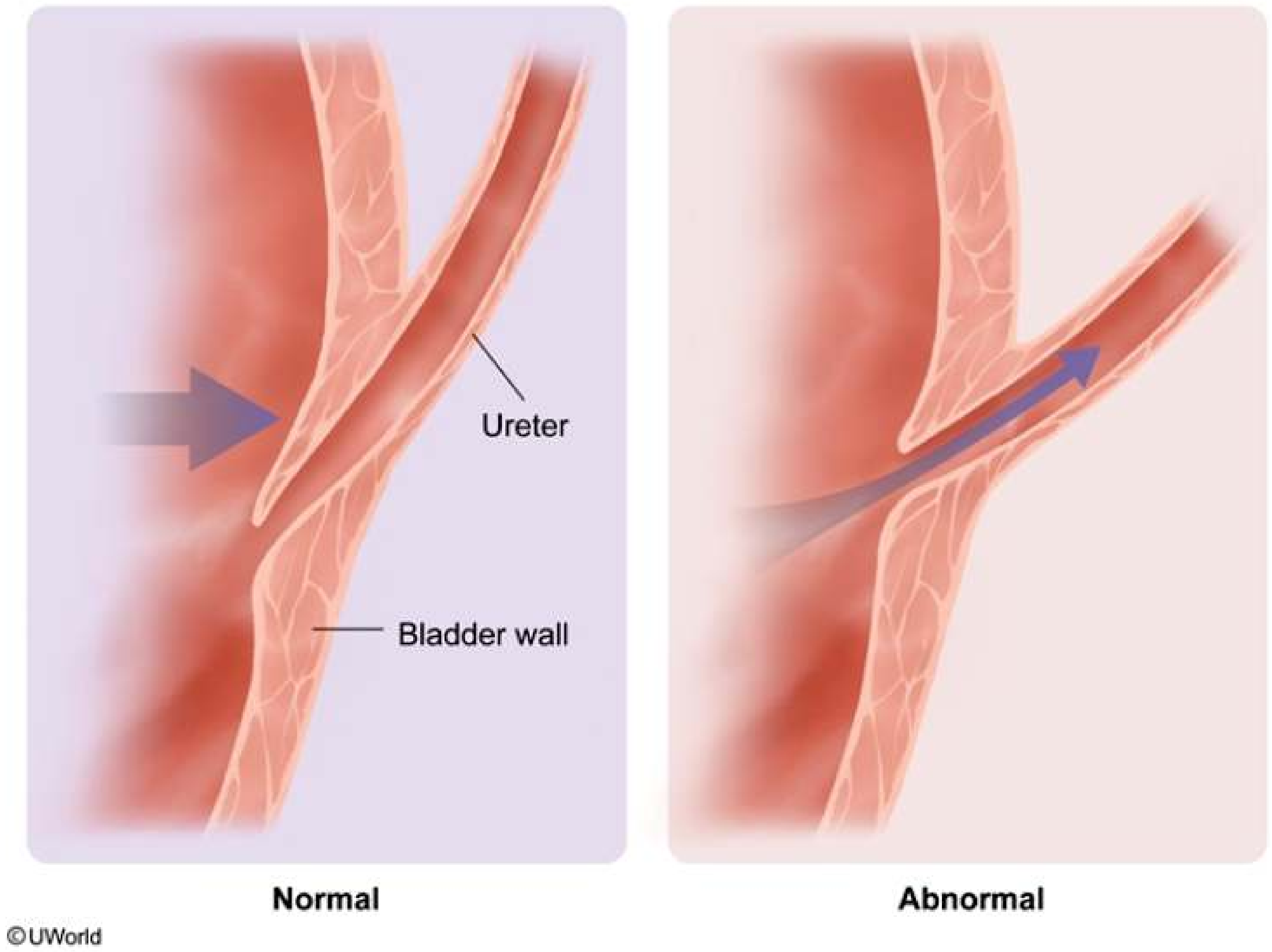
Vesicoureteral reflux



Normal **Abnormal**

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Educational objective:

Retrograde urine flow through the ureterovesical junction, either due to anatomic abnormalities (eg, short

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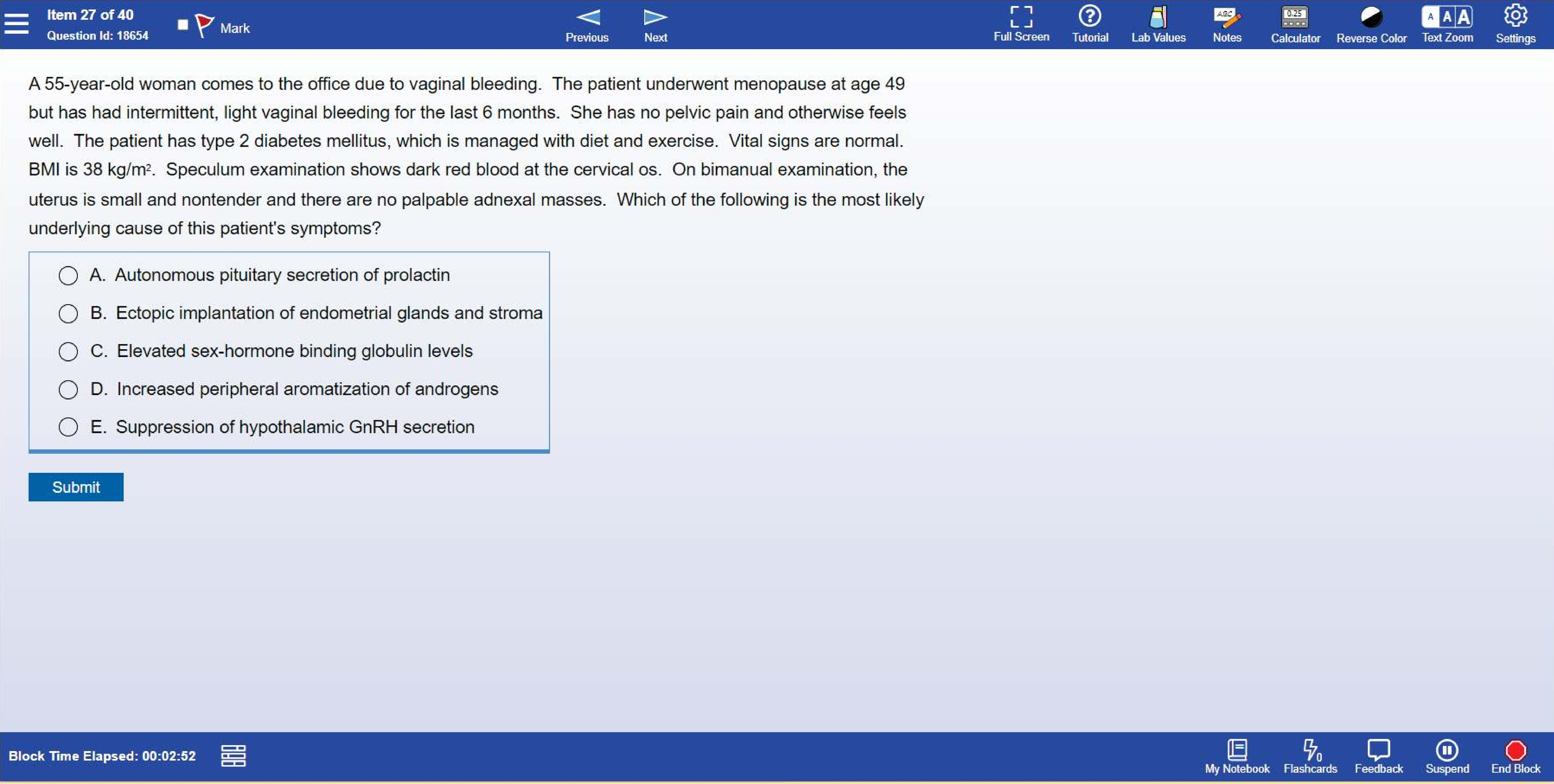
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A 55-year-old woman comes to the office due to vaginal bleeding. The patient underwent menopause at age 49 but has had intermittent, light vaginal bleeding for the last 6 months. She has no pelvic pain and otherwise feels well. The patient has type 2 diabetes mellitus, which is managed with diet and exercise. Vital signs are normal. BMI is 38 kg/m^2. Speculum examination shows dark red blood at the cervical os. On bimanual examination, the uterus is small and nontender and there are no palpable adnexal masses. Which of the following is the most likely underlying cause of this patient's symptoms?

- ○ A. Autonomous pituitary secretion of prolactin
- ○ B. Ectopic implantation of endometrial glands and stroma
- ○ C. Elevated sex-hormone binding globulin levels
- ○ D. Increased peripheral aromatization of androgens
- ○ E. Suppression of hypothalamic GnRH secretion

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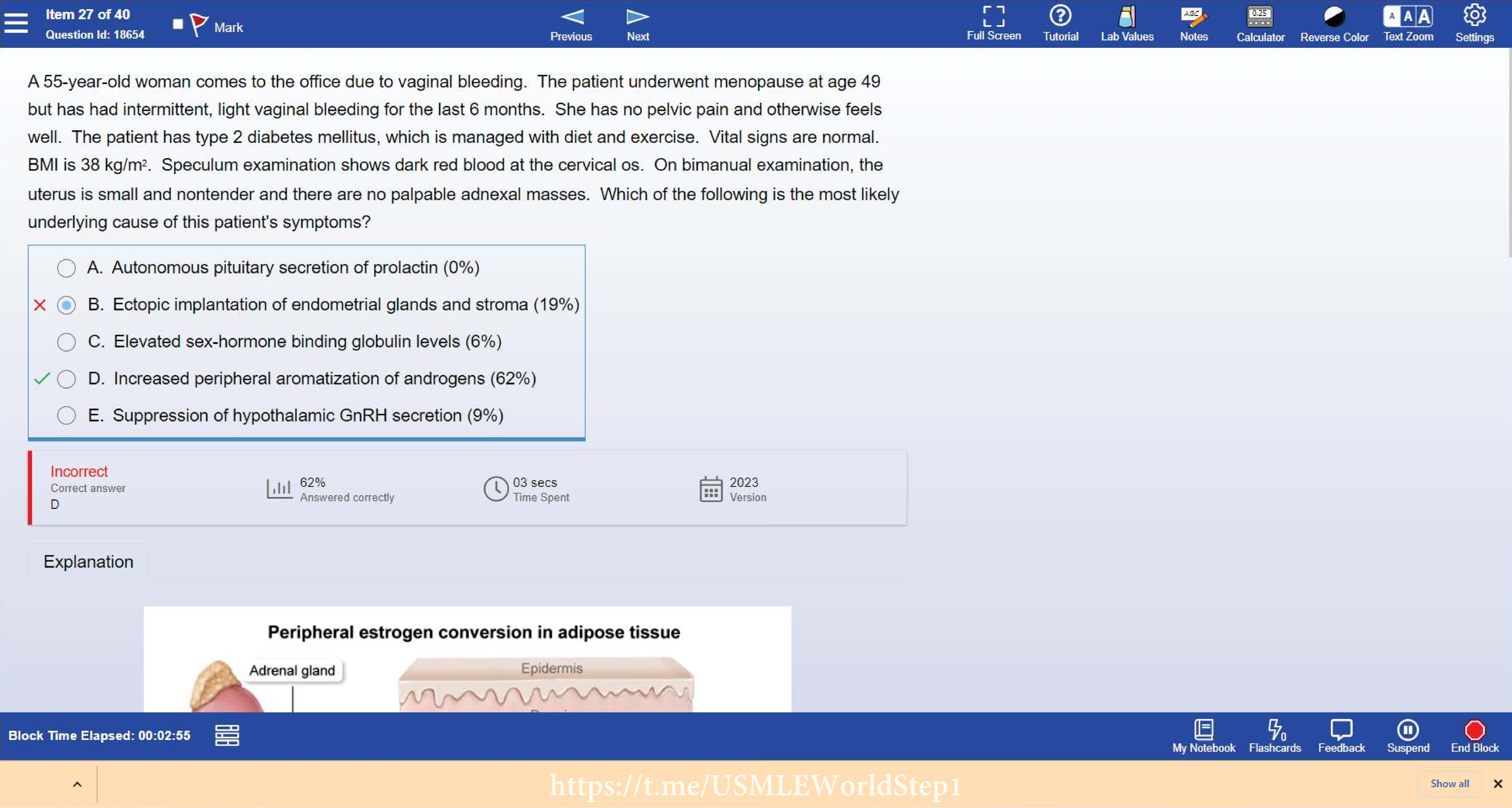
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- ○ A. Autonomous pituitary secretion of prolactin (0%)
- ✗ ● B. Ectopic implantation of endometrial glands and stroma (19%)
- ○ C. Elevated sex-hormone binding globulin levels (6%)
- ✓ ○ D. Increased peripheral aromatization of androgens (62%)
- ○ E. Suppression of hypothalamic GnRH secretion (9%)

Incorrect
Correct answer
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62%
Answered correctly

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Explanation

Peripheral estrogen conversion in adipose tissue

Adrenal gland
Epidermis
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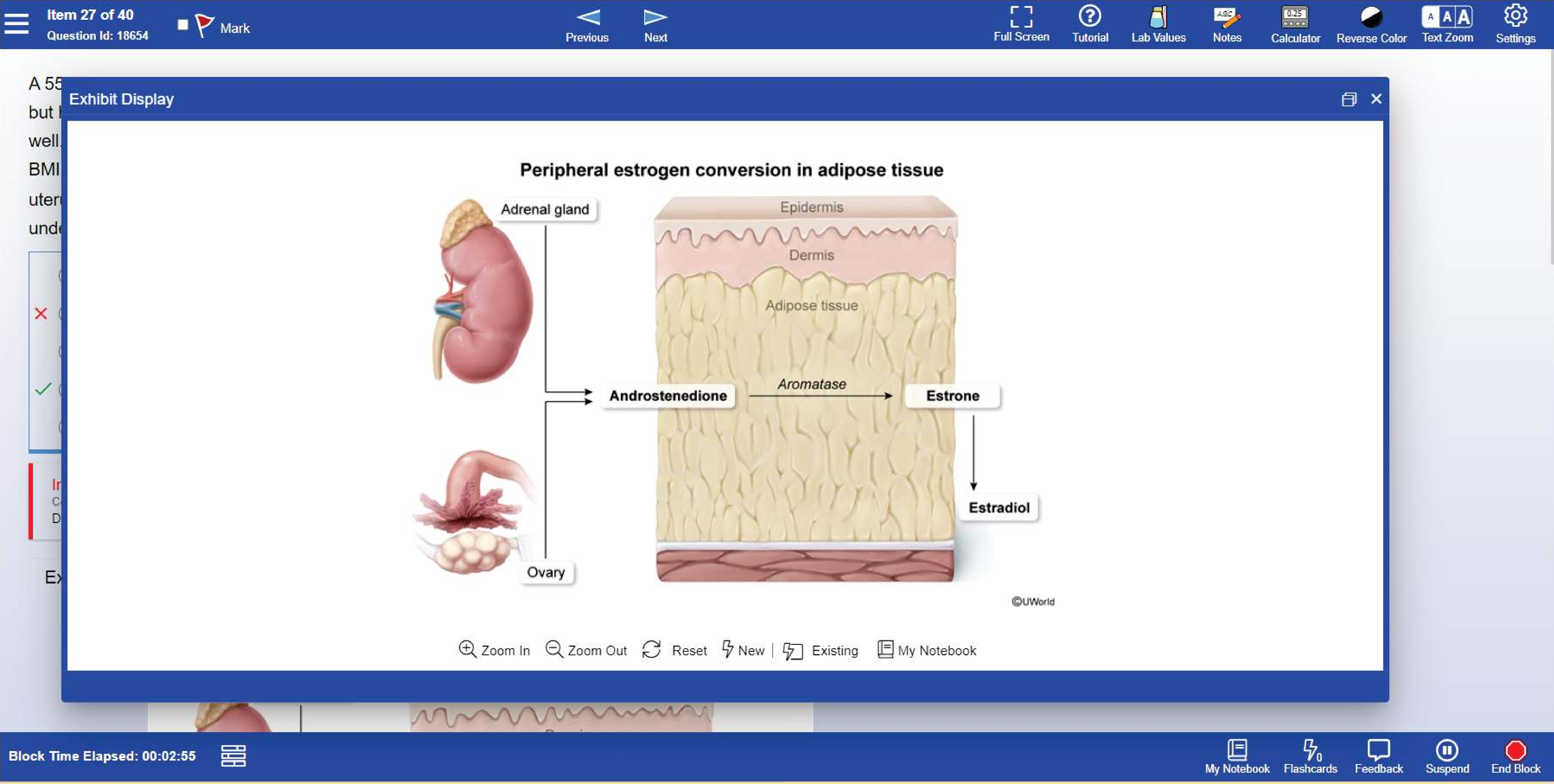

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Peripheral estrogen conversion in adipose tissue

Adrenal gland
Ovary
Epidermis
Dermis
Adipose tissue
Androstenedione
Aromatase
Estrone
Estradiol
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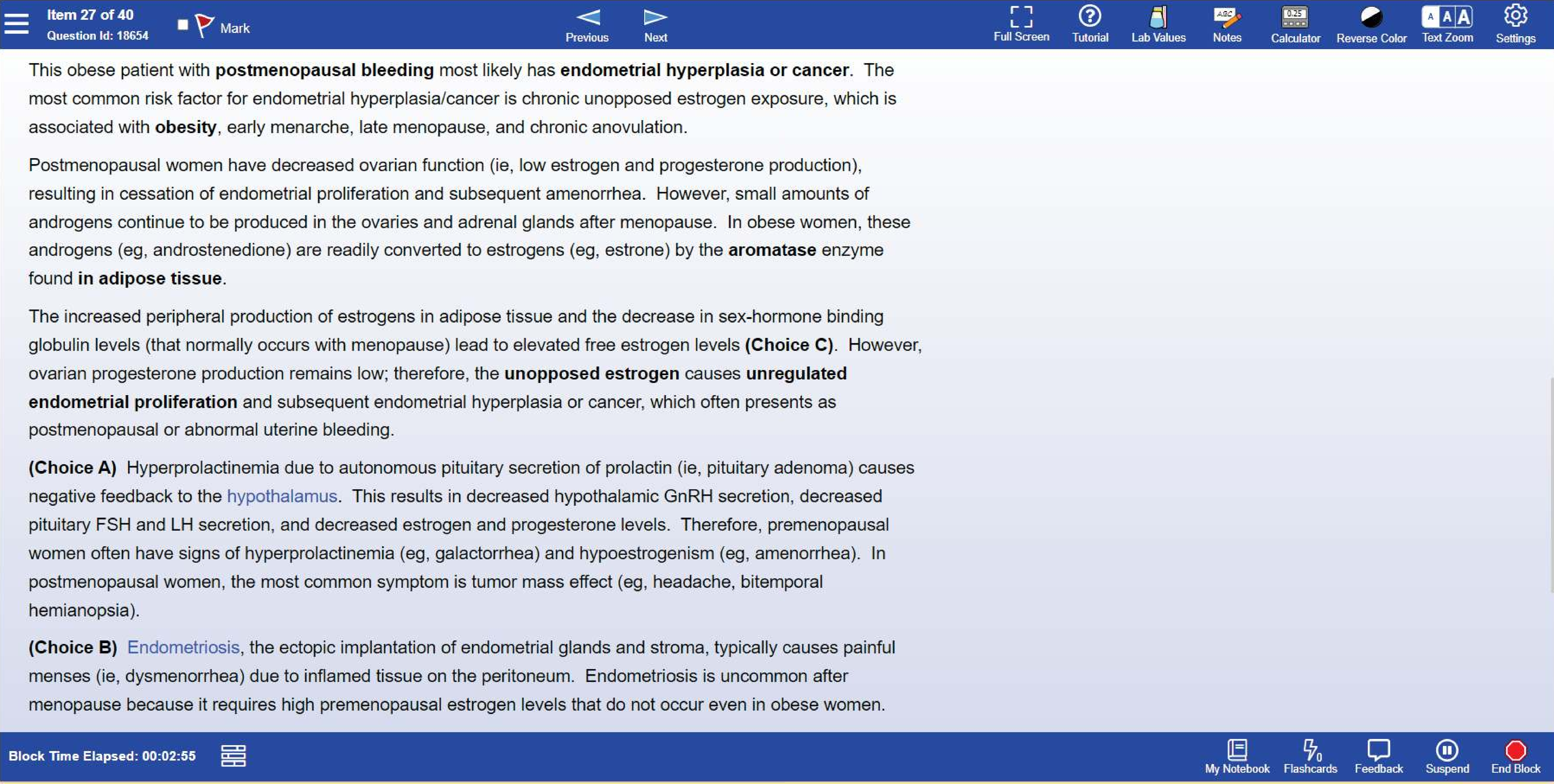


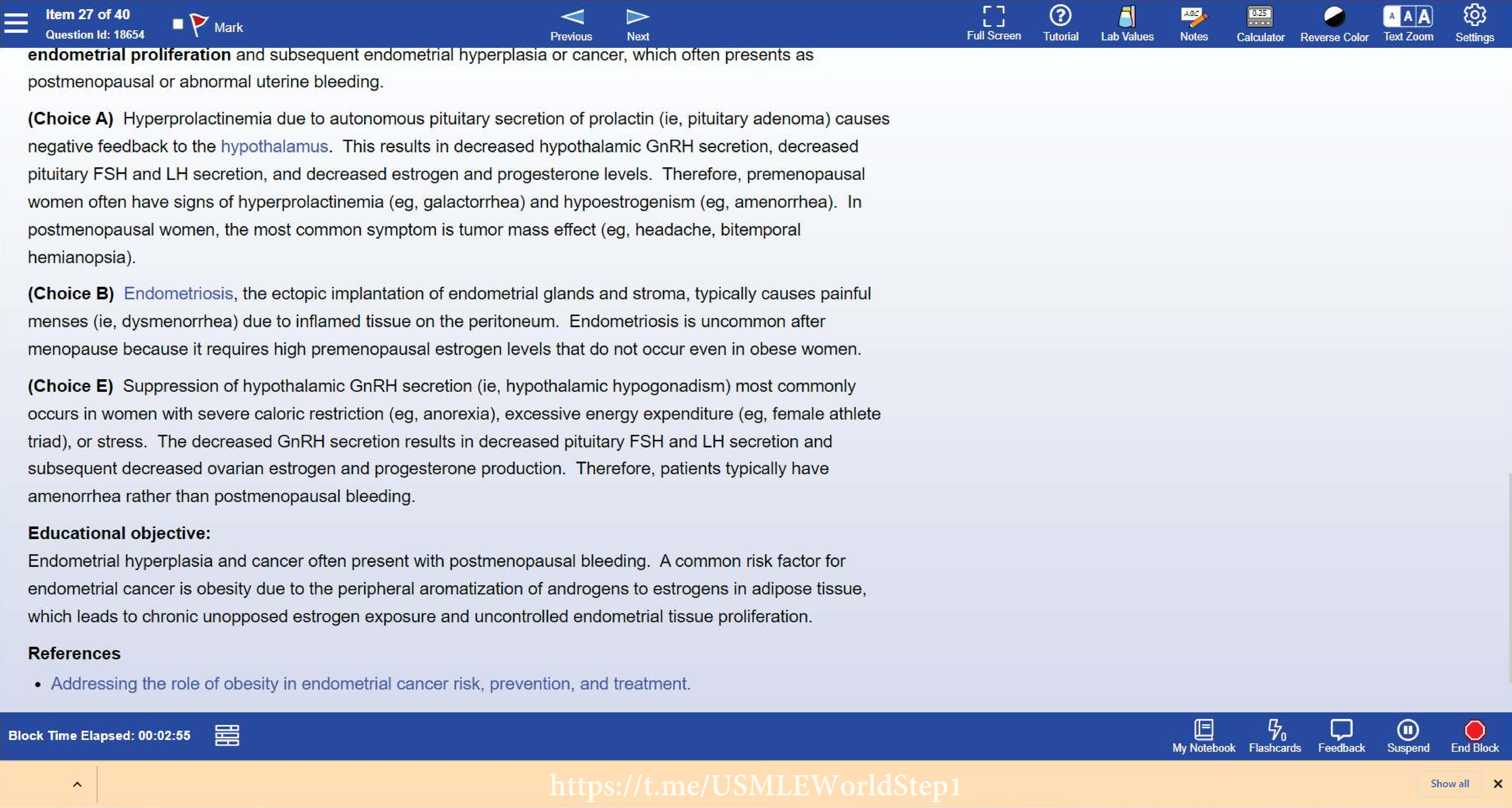
This obese patient with **postmenopausal bleeding** most likely has **endometrial hyperplasia or cancer**. The most common risk factor for endometrial hyperplasia/cancer is chronic unopposed estrogen exposure, which is associated with **obesity**, early menarche, late menopause, and chronic anovulation.

Postmenopausal women have decreased ovarian function (ie, low estrogen and progesterone production), resulting in cessation of endometrial proliferation and subsequent amenorrhea. However, small amounts of androgens continue to be produced in the ovaries and adrenal glands after menopause. In obese women, these androgens (eg, androstenedione) are readily converted to estrogens (eg, estrone) by the **aromatase** enzyme found **in adipose tissue**.

The increased peripheral production of estrogens in adipose tissue and the decrease in sex-hormone binding globulin levels (that normally occurs with menopause) lead to elevated free estrogen levels **(Choice C)**. However, ovarian progesterone production remains low; therefore, the **unopposed estrogen** causes **unregulated endometrial proliferation** and subsequent endometrial hyperplasia or cancer, which often presents as postmenopausal or abnormal uterine bleeding.

(Choice A) Hyperprolactinemia due to autonomous pituitary secretion of prolactin (ie, pituitary adenoma) causes negative feedback to the hypothalamus. This results in decreased hypothalamic GnRH secretion, decreased pituitary FSH and LH secretion, and decreased estrogen and progesterone levels. Therefore, premenopausal women often have signs of hyperprolactinemia (eg, galactorrhea) and hypoestrogenism (eg, amenorrhea). In postmenopausal women, the most common symptom is tumor mass effect (eg, headache, bitemporal hemianopsia).

(Choice B) Endometriosis, the ectopic implantation of endometrial glands and stroma, typically causes painful menses (ie, dysmenorrhea) due to inflamed tissue on the peritoneum. Endometriosis is uncommon after menopause because it requires high premenopausal estrogen levels that do not occur even in obese women.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(Choice E) Suppression of hypothalamic GnRH secretion (ie, hypothalamic hypogonadism) most commonly occurs in women with severe caloric restriction (eg, anorexia), excessive energy expenditure (eg, female athlete triad), or stress. The decreased GnRH secretion results in decreased pituitary FSH and LH secretion and subsequent decreased ovarian estrogen and progesterone production. Therefore, patients typically have amenorrhea rather than postmenopausal bleeding.

Educational objective:

Endometrial hyperplasia and cancer often present with postmenopausal bleeding. A common risk factor for endometrial cancer is obesity due to the peripheral aromatization of androgens to estrogens in adipose tissue, which leads to chronic unopposed estrogen exposure and uncontrolled endometrial tissue proliferation.

References

- Addressing the role of obesity in endometrial cancer risk, prevention, and treatment.

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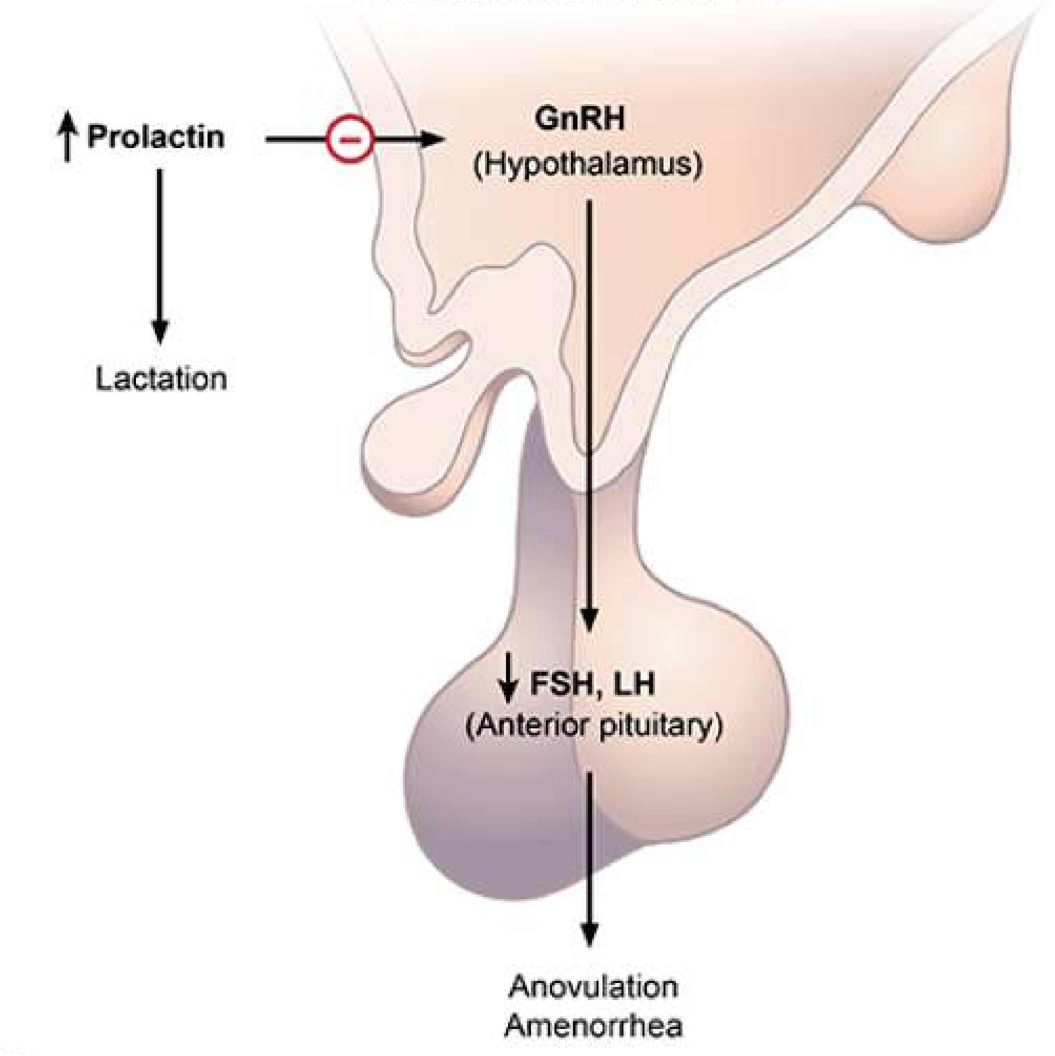
Prolactin & amenorrhea


↑ Prolactin
⊖
GnRH
(Hypothalamus)
Lactation
↓ FSH, LH
(Anterior pituitary)
Anovulation
Amenorrhea

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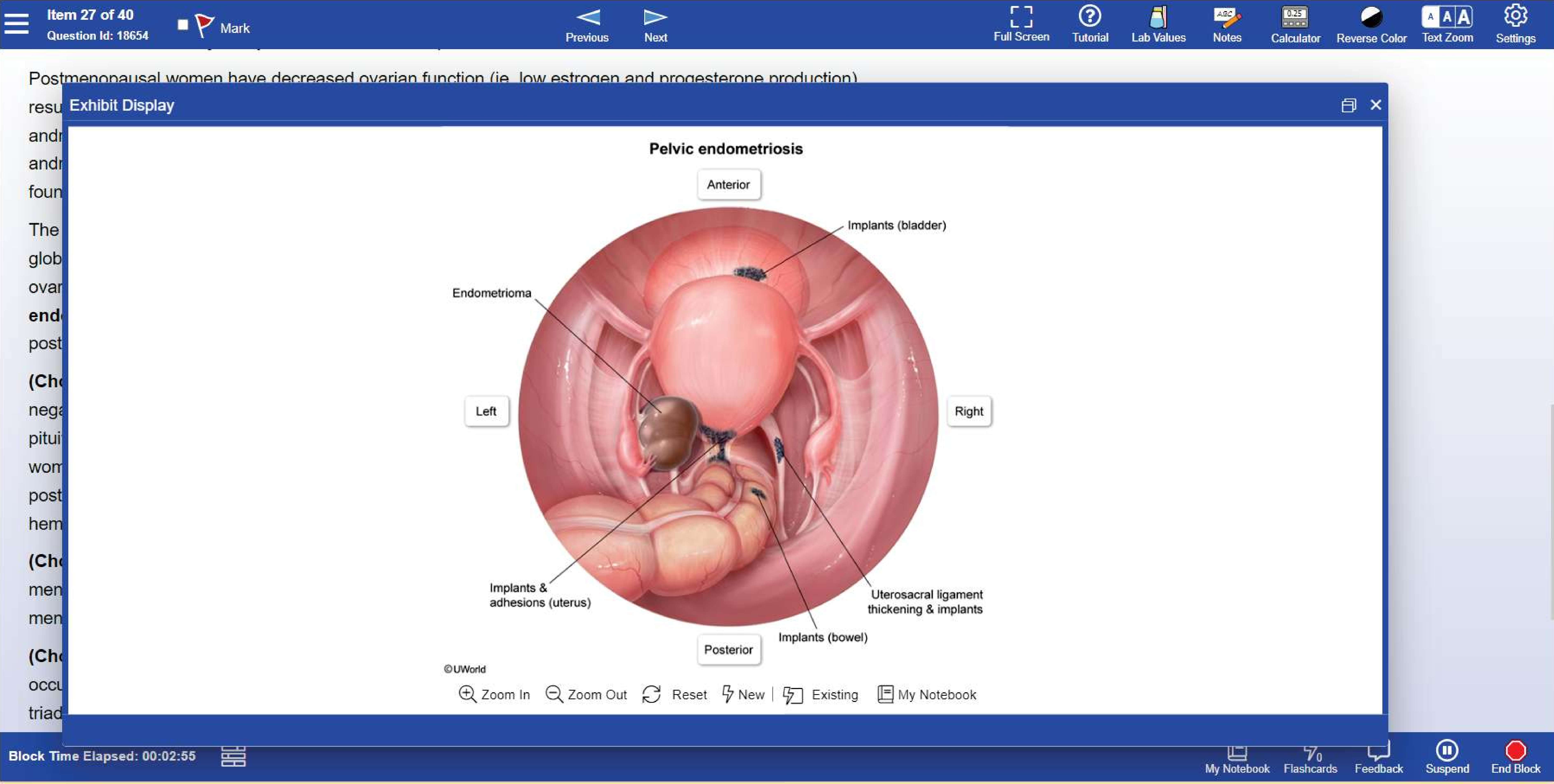
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Postmenopausal women have decreased ovarian function (ie, low estrogen and progesterone production)

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Implants & adhesions (uterus)
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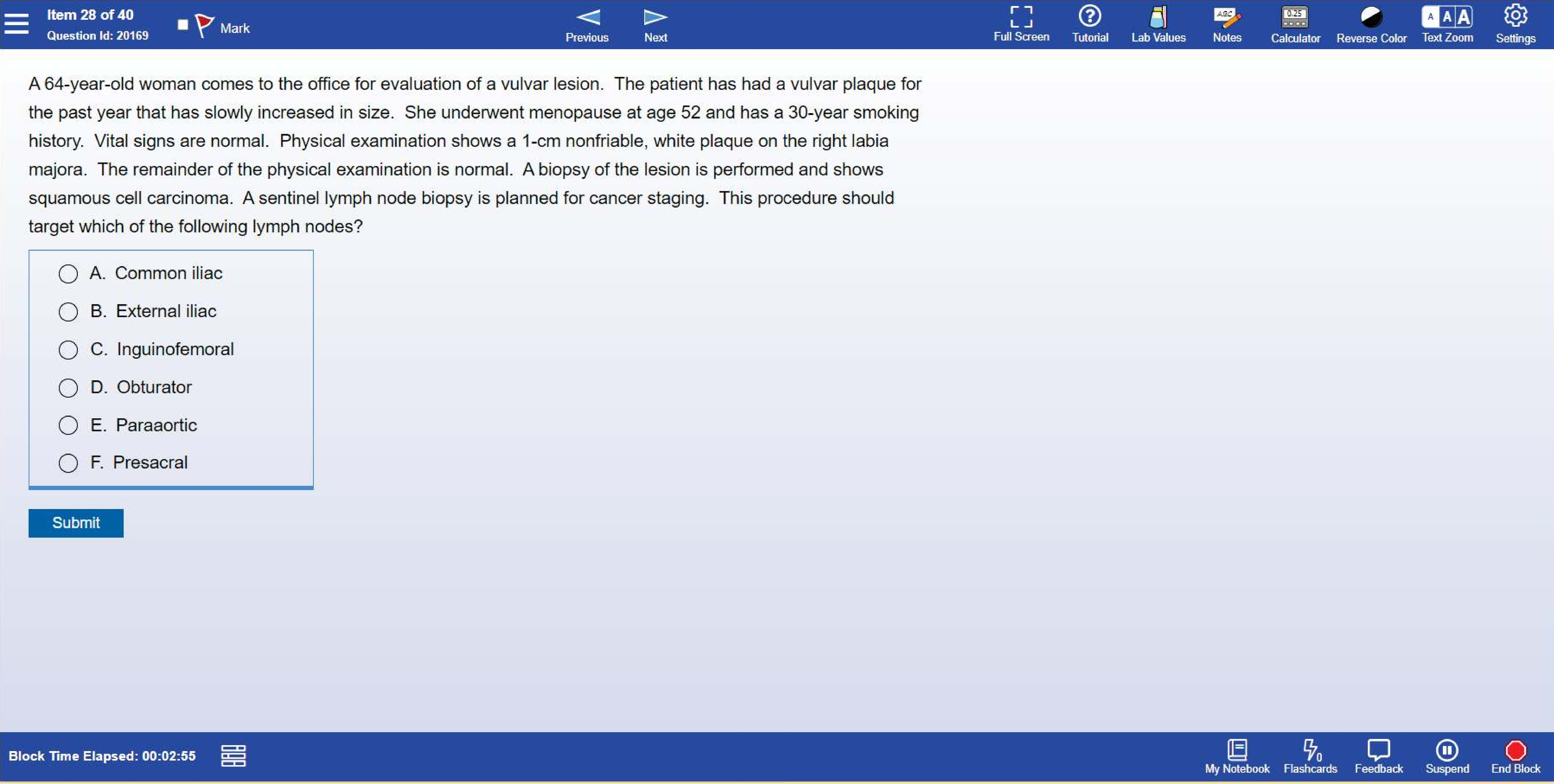

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A 64-year-old woman comes to the office for evaluation of a vulvar lesion. The patient has had a vulvar plaque for the past year that has slowly increased in size. She underwent menopause at age 52 and has a 30-year smoking history. Vital signs are normal. Physical examination shows a 1-cm nonfriable, white plaque on the right labia majora. The remainder of the physical examination is normal. A biopsy of the lesion is performed and shows squamous cell carcinoma. A sentinel lymph node biopsy is planned for cancer staging. This procedure should target which of the following lymph nodes?

○ A. Common iliac
○ B. External iliac
○ C. Inguinofemoral
○ D. Obturator
○ E. Paraaortic
○ F. Presacral

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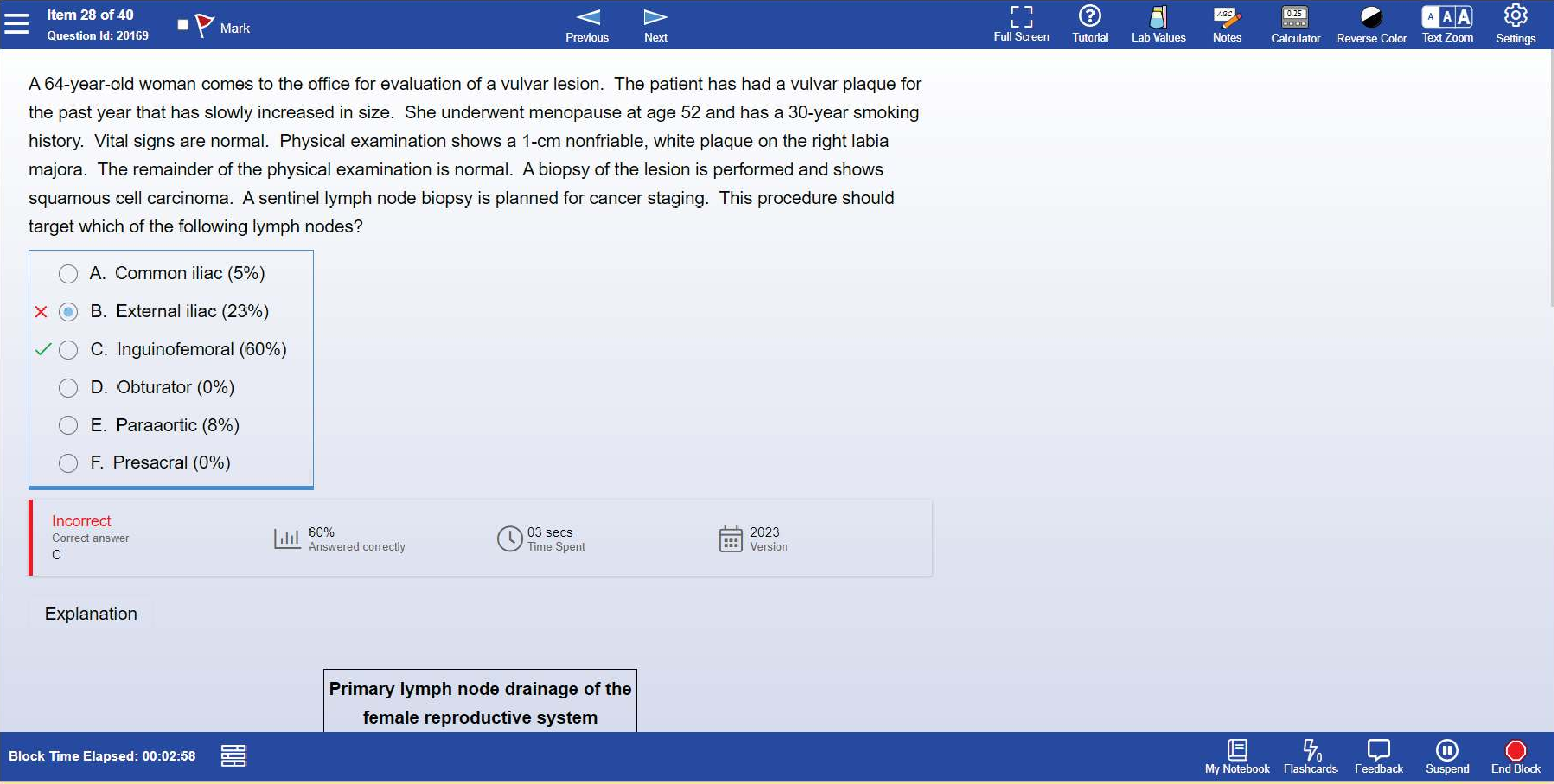
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- ○ A. Common iliac (5%)
- ✗ ● B. External iliac (23%)
- ✓ ○ C. Inguinofemoral (60%)
- ○ D. Obturator (0%)
- ○ E. Paraaortic (8%)
- ○ F. Presacral (0%)

Incorrect
Correct answer
C

60%
Answered correctly

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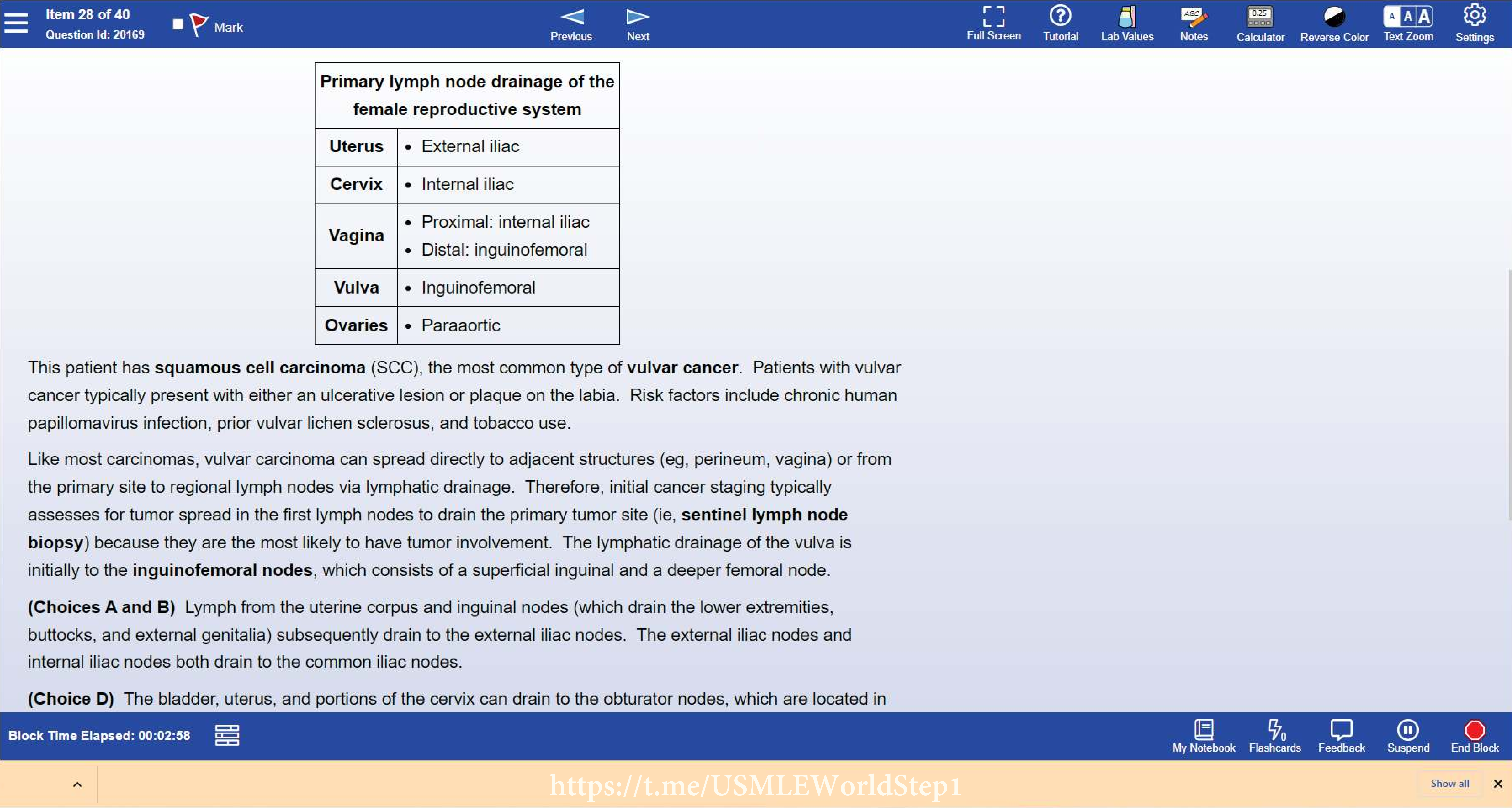
Explanation

Primary lymph node drainage of the female reproductive system



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Primary lymph node drainage of the female reproductive system	
Uterus	- External iliac
Cervix	- Internal iliac
Vagina	- Proximal: internal iliac - Distal: inguinofemoral
Vulva	- Inguinofemoral
Ovaries	- Paraaortic

This patient has **squamous cell carcinoma** (SCC), the most common type of **vulvar cancer**. Patients with vulvar cancer typically present with either an ulcerative lesion or plaque on the labia. Risk factors include chronic human papillomavirus infection, prior vulvar lichen sclerosus, and tobacco use.

Like most carcinomas, vulvar carcinoma can spread directly to adjacent structures (eg, perineum, vagina) or from the primary site to regional lymph nodes via lymphatic drainage. Therefore, initial cancer staging typically assesses for tumor spread in the first lymph nodes to drain the primary tumor site (ie, **sentinel lymph node biopsy**) because they are the most likely to have tumor involvement. The lymphatic drainage of the vulva is initially to the **inguinofemoral nodes**, which consists of a superficial inguinal and a deeper femoral node.

(Choices A and B) Lymph from the uterine corpus and inguinal nodes (which drain the lower extremities, buttocks, and external genitalia) subsequently drain to the external iliac nodes. The external iliac nodes and internal iliac nodes both drain to the common iliac nodes.

(Choice D) The bladder, uterus, and portions of the cervix can drain to the obturator nodes, which are located in

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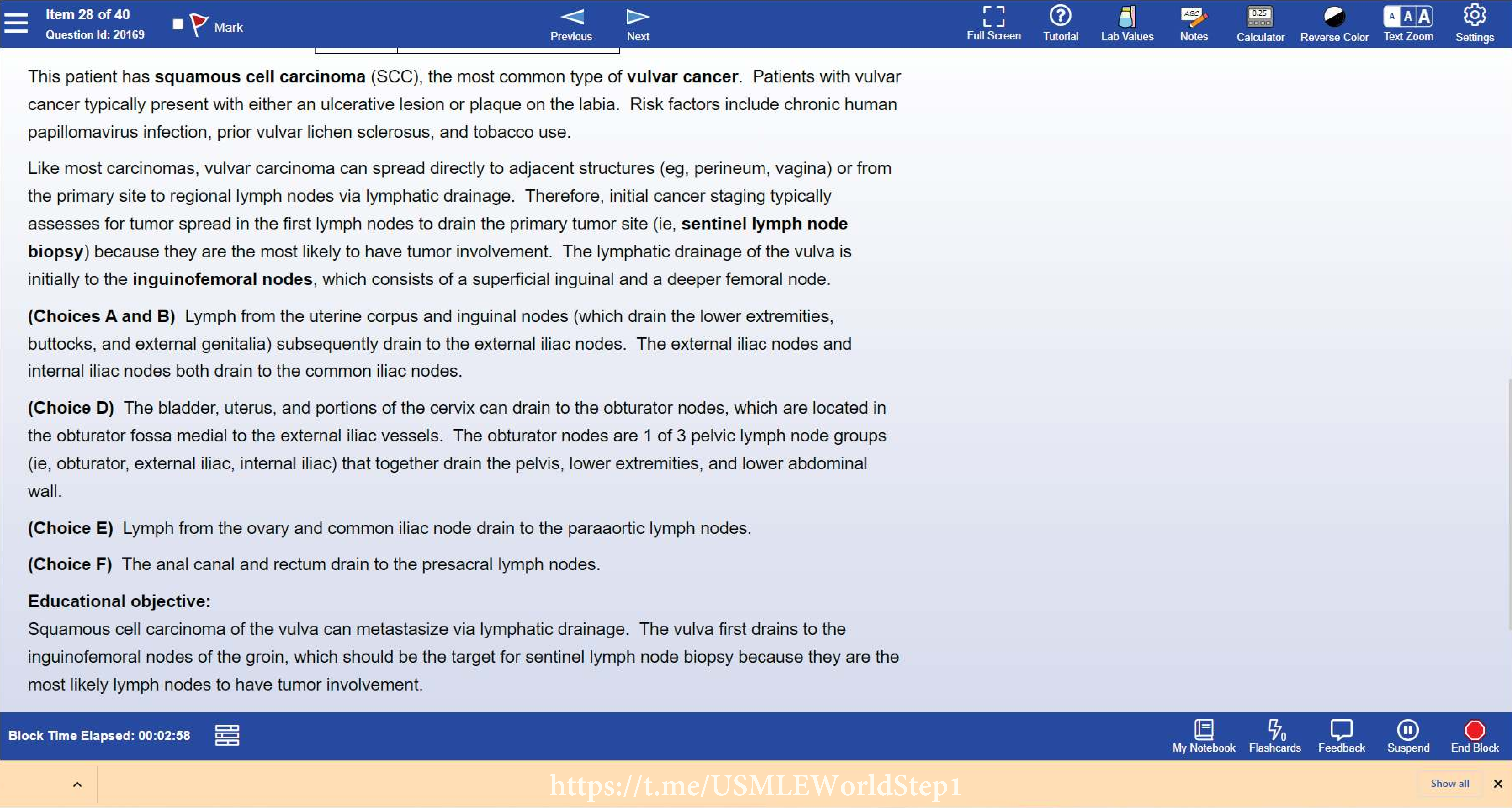
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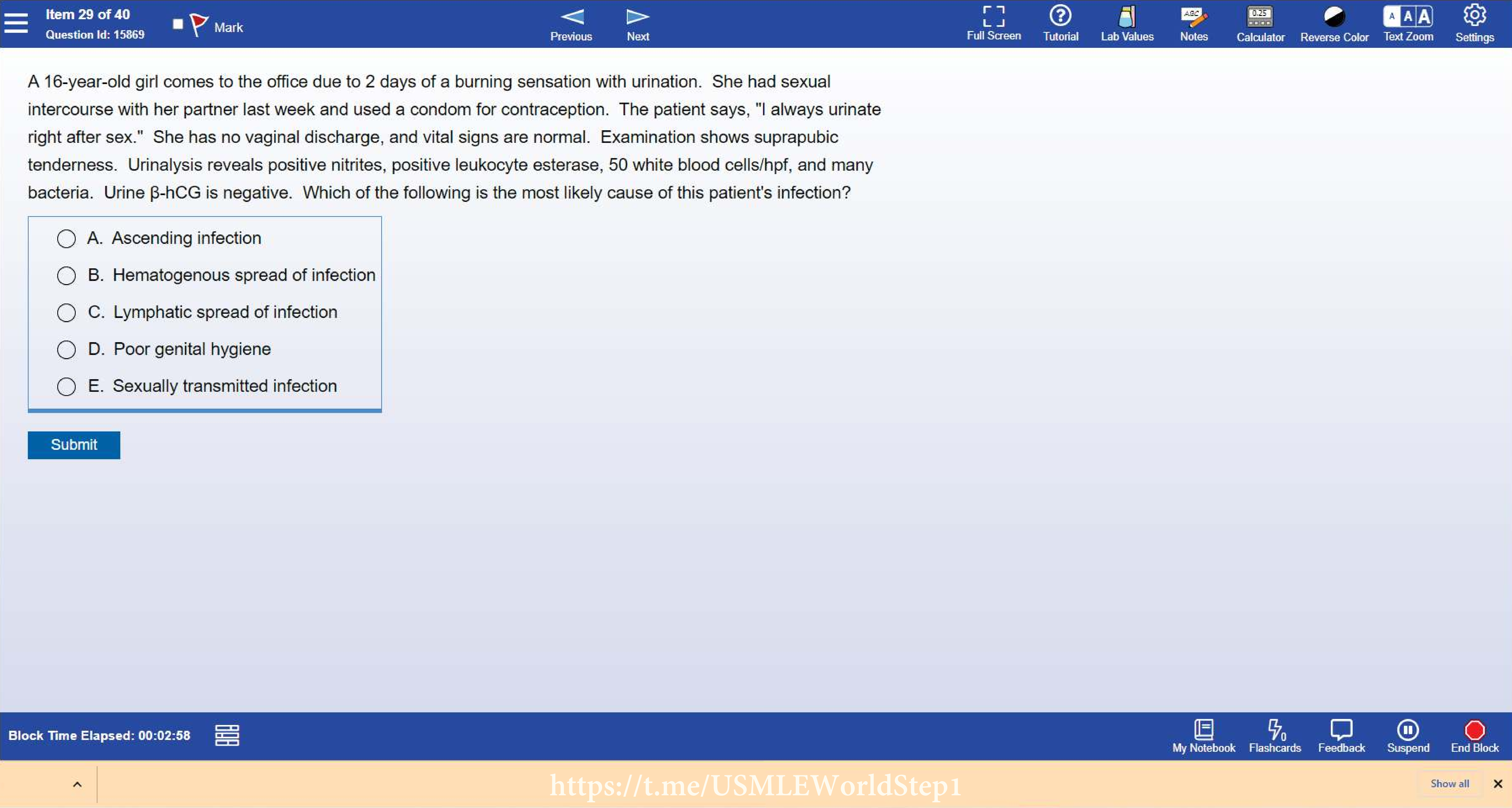
(Choice D) The bladder, uterus, and portions of the cervix can drain to the obturator nodes, which are located in the obturator fossa medial to the external iliac vessels. The obturator nodes are 1 of 3 pelvic lymph node groups (ie, obturator, external iliac, internal iliac) that together drain the pelvis, lower extremities, and lower abdominal wall.

(Choice E) Lymph from the ovary and common iliac node drain to the paraaortic lymph nodes.

(Choice F) The anal canal and rectum drain to the presacral lymph nodes.

Educational objective:
Squamous cell carcinoma of the vulva can metastasize via lymphatic drainage. The vulva first drains to the inguinofemoral nodes of the groin, which should be the target for sentinel lymph node biopsy because they are the most likely lymph nodes to have tumor involvement.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A 16-year-old girl comes to the office due to 2 days of a burning sensation with urination. She had sexual intercourse with her partner last week and used a condom for contraception. The patient says, "I always urinate right after sex." She has no vaginal discharge, and vital signs are normal. Examination shows suprapubic tenderness. Urinalysis reveals positive nitrites, positive leukocyte esterase, 50 white blood cells/hpf, and many bacteria. Urine β-hCG is negative. Which of the following is the most likely cause of this patient's infection?

- ○ A. Ascending infection
- ○ B. Hematogenous spread of infection
- ○ C. Lymphatic spread of infection
- ○ D. Poor genital hygiene
- ○ E. Sexually transmitted infection

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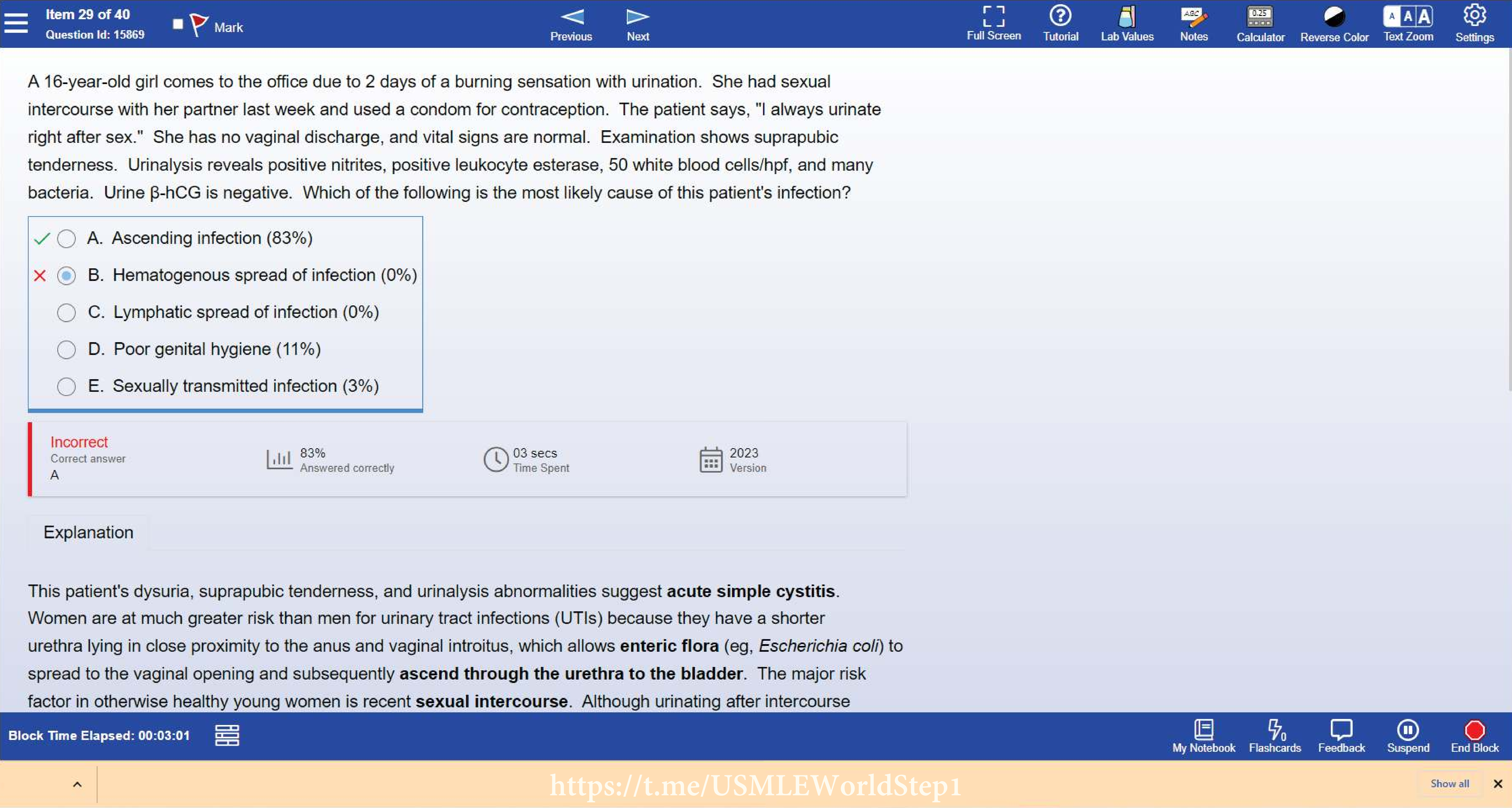
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✓ ○ A. Ascending infection (83%)
✗ ● B. Hematogenous spread of infection (0%)
○ C. Lymphatic spread of infection (0%)
○ D. Poor genital hygiene (11%)
○ E. Sexually transmitted infection (3%)

Incorrect
Correct answer
A

83%
Answered correctly

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Explanation

This patient's dysuria, suprapubic tenderness, and urinalysis abnormalities suggest **acute simple cystitis**. Women are at much greater risk than men for urinary tract infections (UTIs) because they have a shorter urethra lying in close proximity to the anus and vaginal introitus, which allows **enteric flora** (eg, *Escherichia coli*) to spread to the vaginal opening and subsequently **ascend through the urethra to the bladder**. The major risk factor in otherwise healthy young women is recent **sexual intercourse**. Although urinating after intercourse

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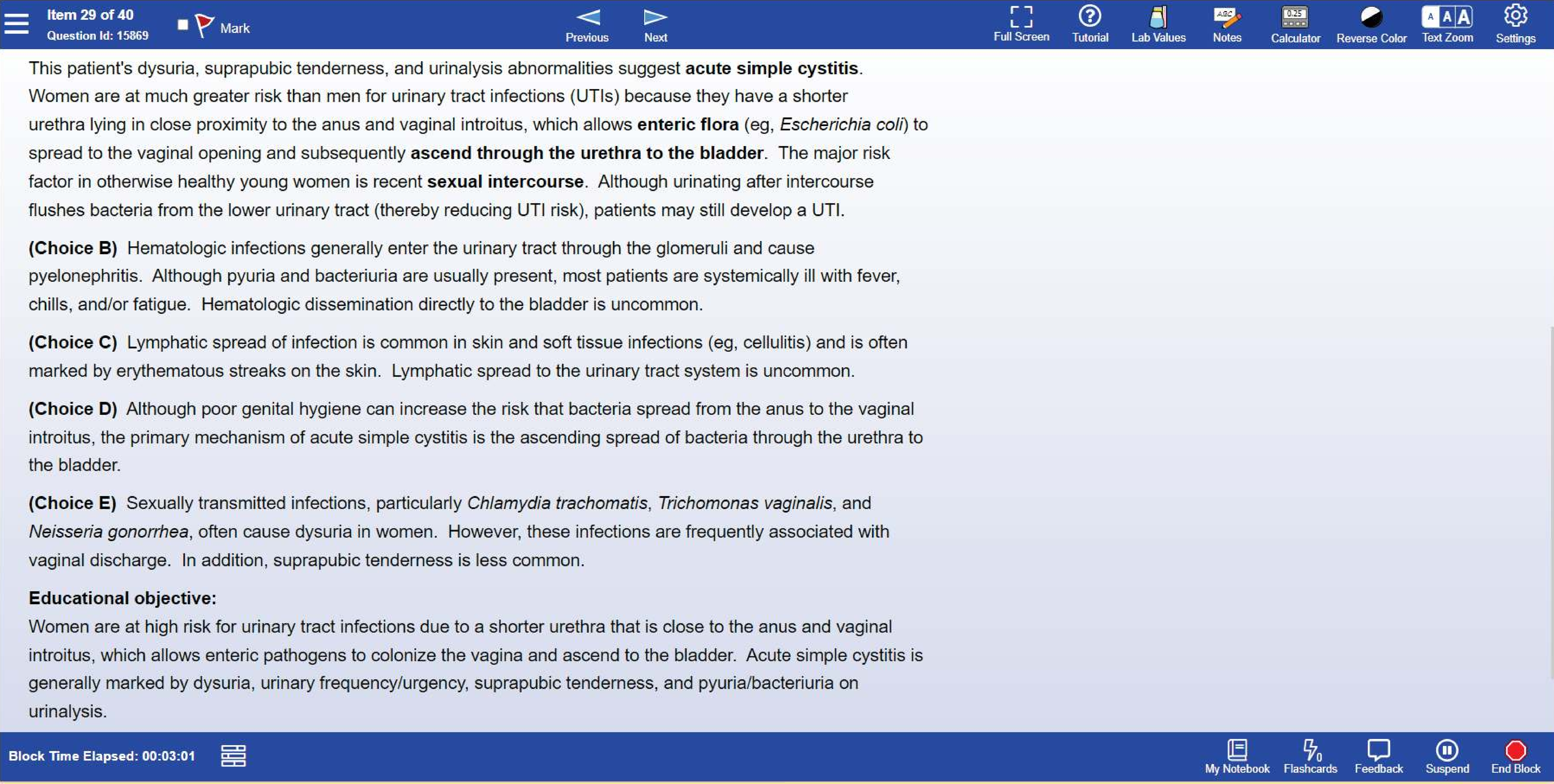

This patient's dysuria, suprapubic tenderness, and urinalysis abnormalities suggest **acute simple cystitis**. Women are at much greater risk than men for urinary tract infections (UTIs) because they have a shorter urethra lying in close proximity to the anus and vaginal introitus, which allows **enteric flora** (eg, *Escherichia coli*) to spread to the vaginal opening and subsequently **ascend through the urethra to the bladder**. The major risk factor in otherwise healthy young women is recent **sexual intercourse**. Although urinating after intercourse flushes bacteria from the lower urinary tract (thereby reducing UTI risk), patients may still develop a UTI.

(Choice B) Hematologic infections generally enter the urinary tract through the glomeruli and cause pyelonephritis. Although pyuria and bacteriuria are usually present, most patients are systemically ill with fever, chills, and/or fatigue. Hematologic dissemination directly to the bladder is uncommon.

(Choice C) Lymphatic spread of infection is common in skin and soft tissue infections (eg, cellulitis) and is often marked by erythematous streaks on the skin. Lymphatic spread to the urinary tract system is uncommon.

(Choice D) Although poor genital hygiene can increase the risk that bacteria spread from the anus to the vaginal introitus, the primary mechanism of acute simple cystitis is the ascending spread of bacteria through the urethra to the bladder.

(Choice E) Sexually transmitted infections, particularly *Chlamydia trachomatis*, *Trichomonas vaginalis*, and *Neisseria gonorrhea*, often cause dysuria in women. However, these infections are frequently associated with vaginal discharge. In addition, suprapubic tenderness is less common.

Educational objective:
Women are at high risk for urinary tract infections due to a shorter urethra that is close to the anus and vaginal introitus, which allows enteric pathogens to colonize the vagina and ascend to the bladder. Acute simple cystitis is generally marked by dysuria, urinary frequency/urgency, suprapubic tenderness, and pyuria/bacteriuria on urinalysis.

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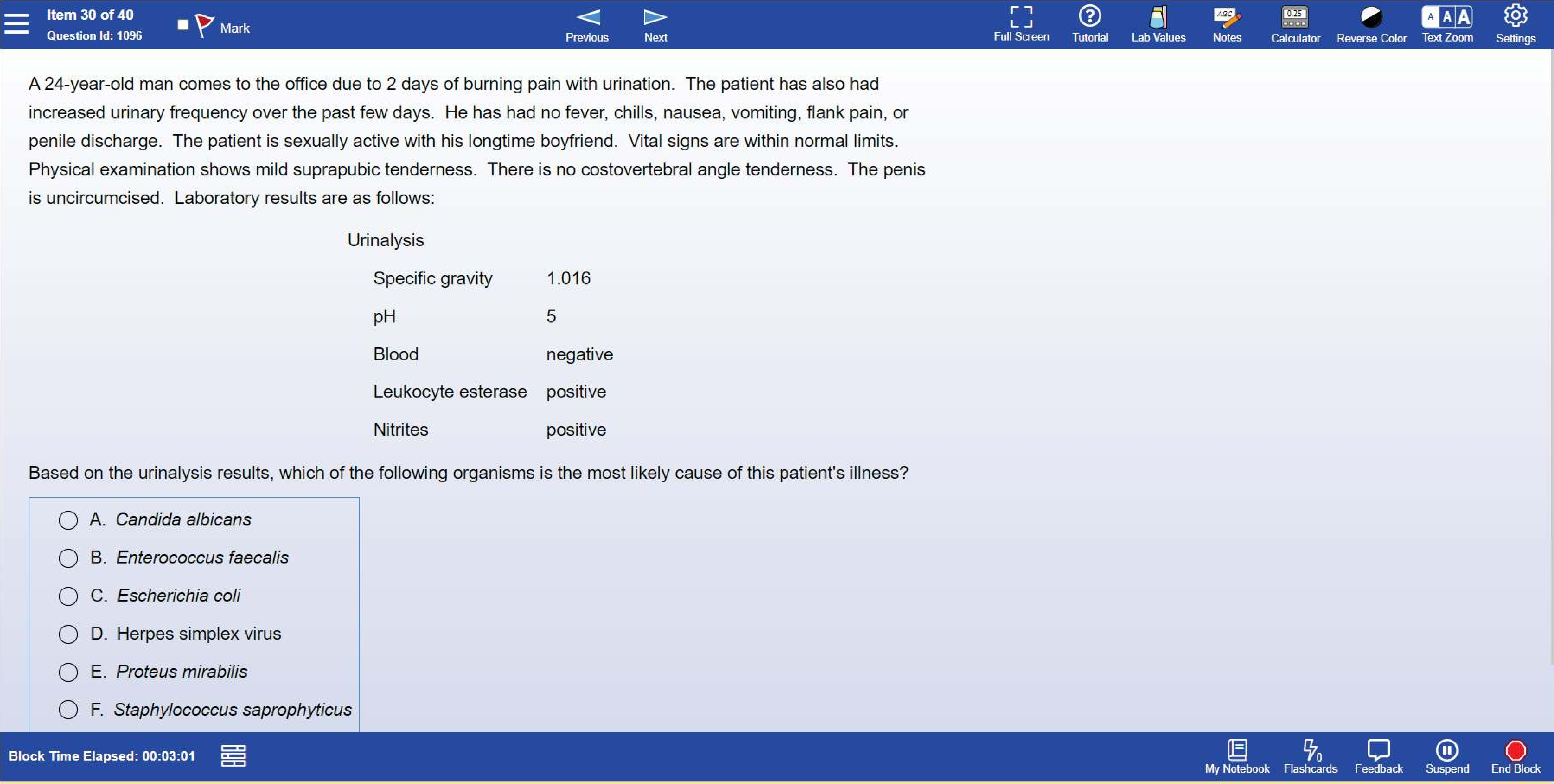
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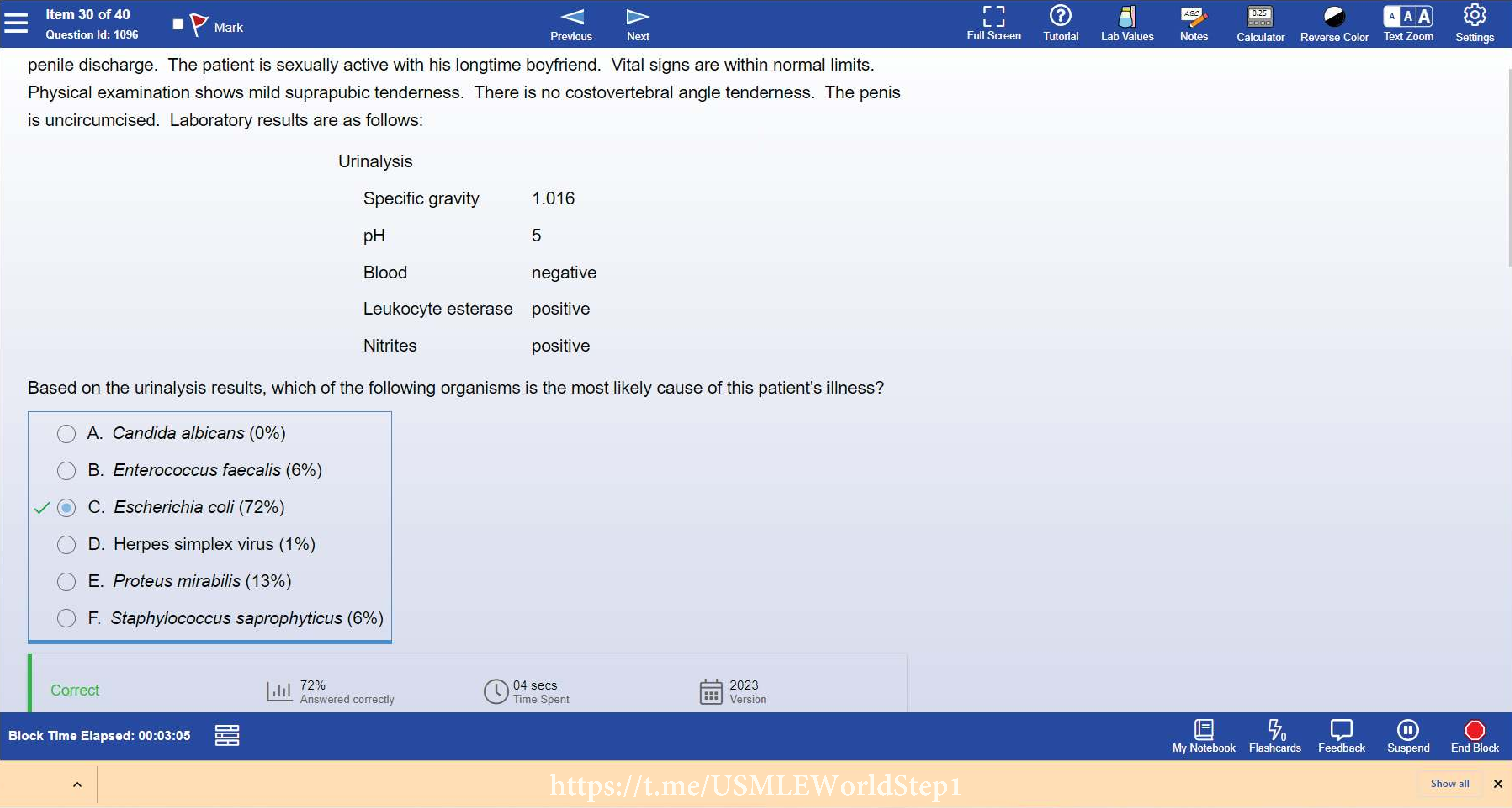
A 24-year-old man comes to the office due to 2 days of burning pain with urination. The patient has also had increased urinary frequency over the past few days. He has had no fever, chills, nausea, vomiting, flank pain, or penile discharge. The patient is sexually active with his longtime boyfriend. Vital signs are within normal limits. Physical examination shows mild suprapubic tenderness. There is no costovertebral angle tenderness. The penis is uncircumcised. Laboratory results are as follows:

Urinalysis	
Specific gravity	1.016
pH	5
Blood	negative
Leukocyte esterase	positive
Nitrites	positive

Based on the urinalysis results, which of the following organisms is the most likely cause of this patient's illness?

○ A. *Candida albicans*
○ B. *Enterococcus faecalis*
○ C. *Escherichia coli*
○ D. Herpes simplex virus
○ E. *Proteus mirabilis*
○ F. *Staphylococcus saprophyticus*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penile discharge. The patient is sexually active with his longtime boyfriend. Vital signs are within normal limits. Physical examination shows mild suprapubic tenderness. There is no costovertebral angle tenderness. The penis is uncircumcised. Laboratory results are as follows:

Urinalysis	
Specific gravity	1.016
pH	5
Blood	negative
Leukocyte esterase	positive
Nitrites	positive

Based on the urinalysis results, which of the following organisms is the most likely cause of this patient's illness?

- ○ A. *Candida albicans* (0%)
- ○ B. *Enterococcus faecalis* (6%)
- ✓ ● C. *Escherichia coli* (72%)
- ○ D. Herpes simplex virus (1%)
- ○ E. *Proteus mirabilis* (13%)
- ○ F. *Staphylococcus saprophyticus* (6%)

Correct

72% Answered correctly

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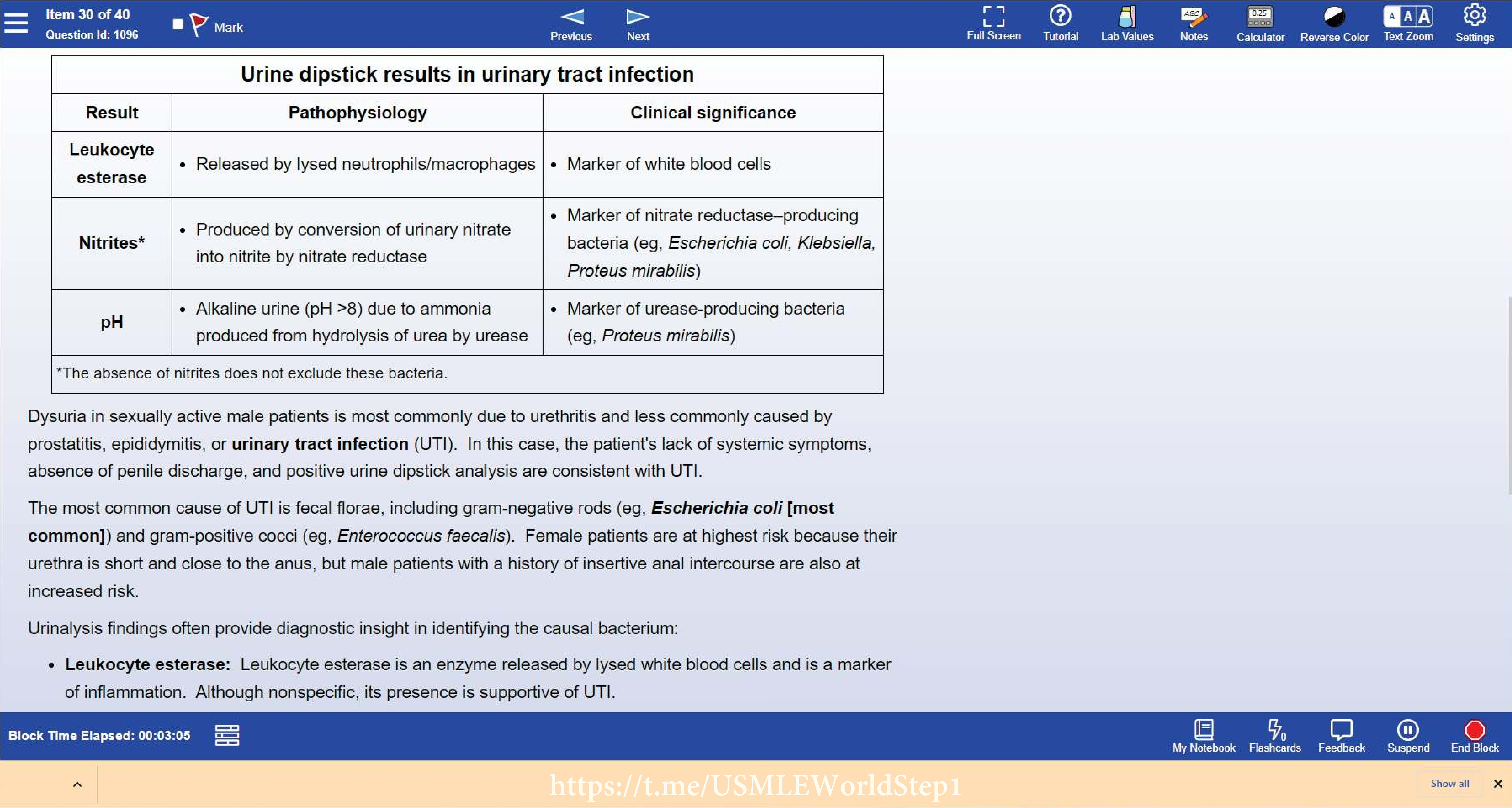
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Urine dipstick results in urinary tract infection		
Result	**Pathophysiology**	**Clinical significance**
Leukocyte esterase	- Released by lysed neutrophils/macrophages	- Marker of white blood cells
Nitrites*	- Produced by conversion of urinary nitrate into nitrite by nitrate reductase	- Marker of nitrate reductase–producing bacteria (eg, *Escherichia coli, Klebsiella, Proteus mirabilis*)
pH	- Alkaline urine (pH >8) due to ammonia produced from hydrolysis of urea by urease	- Marker of urease-producing bacteria (eg, *Proteus mirabilis*)
*The absence of nitrites does not exclude these bacteria.		

Dysuria in sexually active male patients is most commonly due to urethritis and less commonly caused by prostatitis, epididymitis, or **urinary tract infection** (UTI). In this case, the patient's lack of systemic symptoms, absence of penile discharge, and positive urine dipstick analysis are consistent with UTI.

The most common cause of UTI is fecal florae, including gram-negative rods (eg, ***Escherichia coli* [most common]**) and gram-positive cocci (eg, *Enterococcus faecalis*). Female patients are at highest risk because their urethra is short and close to the anus, but male patients with a history of insertive anal intercourse are also at increased risk.

Urinalysis findings often provide diagnostic insight in identifying the causal bacterium:

- **Leukocyte esterase:** Leukocyte esterase is an enzyme released by lysed white blood cells and is a marker of inflammation. Although nonspecific, its presence is supportive of UTI.

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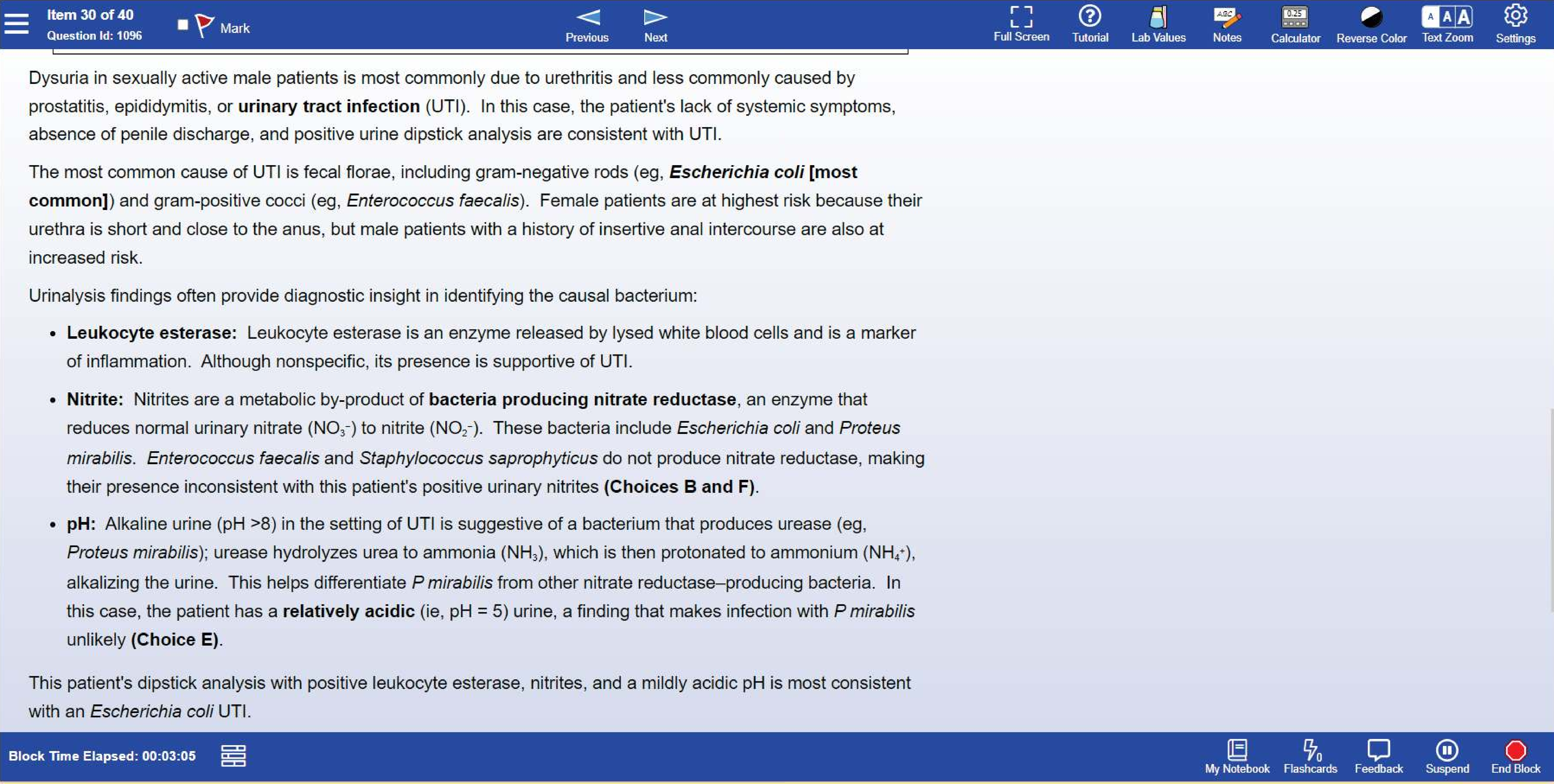
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Dysuria in sexually active male patients is most commonly due to urethritis and less commonly caused by prostatitis, epididymitis, or **urinary tract infection** (UTI). In this case, the patient's lack of systemic symptoms, absence of penile discharge, and positive urine dipstick analysis are consistent with UTI.

The most common cause of UTI is fecal florae, including gram-negative rods (eg, ***Escherichia coli* [most common]**) and gram-positive cocci (eg, *Enterococcus faecalis*). Female patients are at highest risk because their urethra is short and close to the anus, but male patients with a history of insertive anal intercourse are also at increased risk.

Urinalysis findings often provide diagnostic insight in identifying the causal bacterium:

- **Leukocyte esterase:** Leukocyte esterase is an enzyme released by lysed white blood cells and is a marker of inflammation. Although nonspecific, its presence is supportive of UTI.
- **Nitrite:** Nitrites are a metabolic by-product of **bacteria producing nitrate reductase**, an enzyme that reduces normal urinary nitrate (NO_3^-) to nitrite (NO_2^-). These bacteria include *Escherichia coli* and *Proteus mirabilis*. *Enterococcus faecalis* and *Staphylococcus saprophyticus* do not produce nitrate reductase, making their presence inconsistent with this patient's positive urinary nitrites **(Choices B and F)**.
- **pH:** Alkaline urine (pH >8) in the setting of UTI is suggestive of a bacterium that produces urease (eg, *Proteus mirabilis*); urease hydrolyzes urea to ammonia (NH_3), which is then protonated to ammonium (NH_4^+), alkalizing the urine. This helps differentiate *P mirabilis* from other nitrate reductase–producing bacteria. In this case, the patient has a **relatively acidic** (ie, pH = 5) urine, a finding that makes infection with *P mirabilis* unlikely **(Choice E)**.

This patient's dipstick analysis with positive leukocyte esterase, nitrites, and a mildly acidic pH is most consistent with an *Escherichia coli* UTI.

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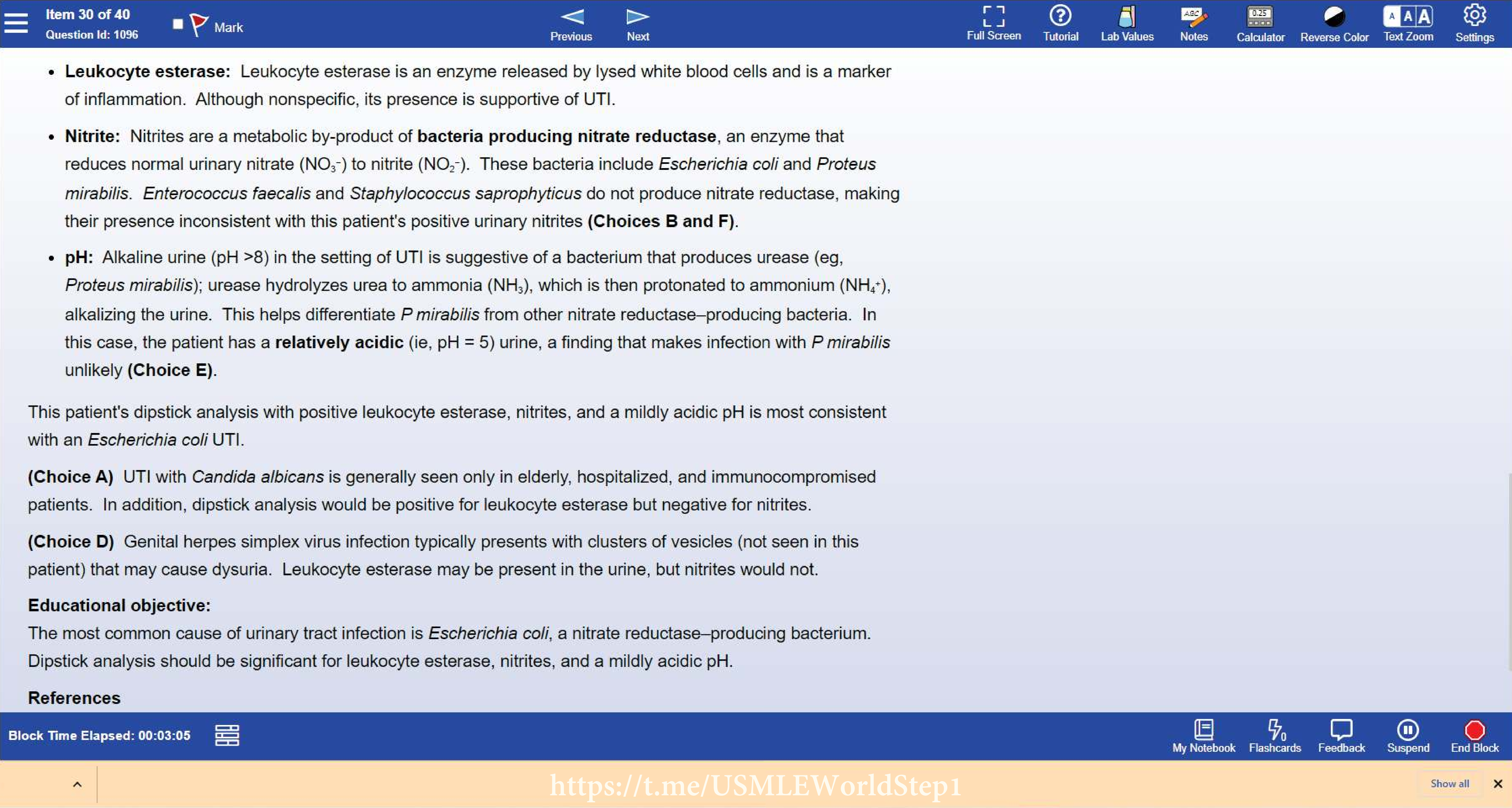
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- **Leukocyte esterase:** Leukocyte esterase is an enzyme released by lysed white blood cells and is a marker of inflammation. Although nonspecific, its presence is supportive of UTI.
- **Nitrite:** Nitrites are a metabolic by-product of **bacteria producing nitrate reductase**, an enzyme that reduces normal urinary nitrate (NO_3^-) to nitrite (NO_2^-). These bacteria include *Escherichia coli* and *Proteus mirabilis*. *Enterococcus faecalis* and *Staphylococcus saprophyticus* do not produce nitrate reductase, making their presence inconsistent with this patient's positive urinary nitrites **(Choices B and F)**.
- **pH:** Alkaline urine (pH >8) in the setting of UTI is suggestive of a bacterium that produces urease (eg, *Proteus mirabilis*); urease hydrolyzes urea to ammonia (NH_3), which is then protonated to ammonium (NH_4^+), alkalizing the urine. This helps differentiate *P mirabilis* from other nitrate reductase–producing bacteria. In this case, the patient has a **relatively acidic** (ie, pH = 5) urine, a finding that makes infection with *P mirabilis* unlikely **(Choice E)**.

This patient's dipstick analysis with positive leukocyte esterase, nitrites, and a mildly acidic pH is most consistent with an *Escherichia coli* UTI.

(Choice A) UTI with *Candida albicans* is generally seen only in elderly, hospitalized, and immunocompromised patients. In addition, dipstick analysis would be positive for leukocyte esterase but negative for nitrites.

(Choice D) Genital herpes simplex virus infection typically presents with clusters of vesicles (not seen in this patient) that may cause dysuria. Leukocyte esterase may be present in the urine, but nitrites would not.

Educational objective:

The most common cause of urinary tract infection is *Escherichia coli*, a nitrate reductase–producing bacterium. Dipstick analysis should be significant for leukocyte esterase, nitrites, and a mildly acidic pH.

References

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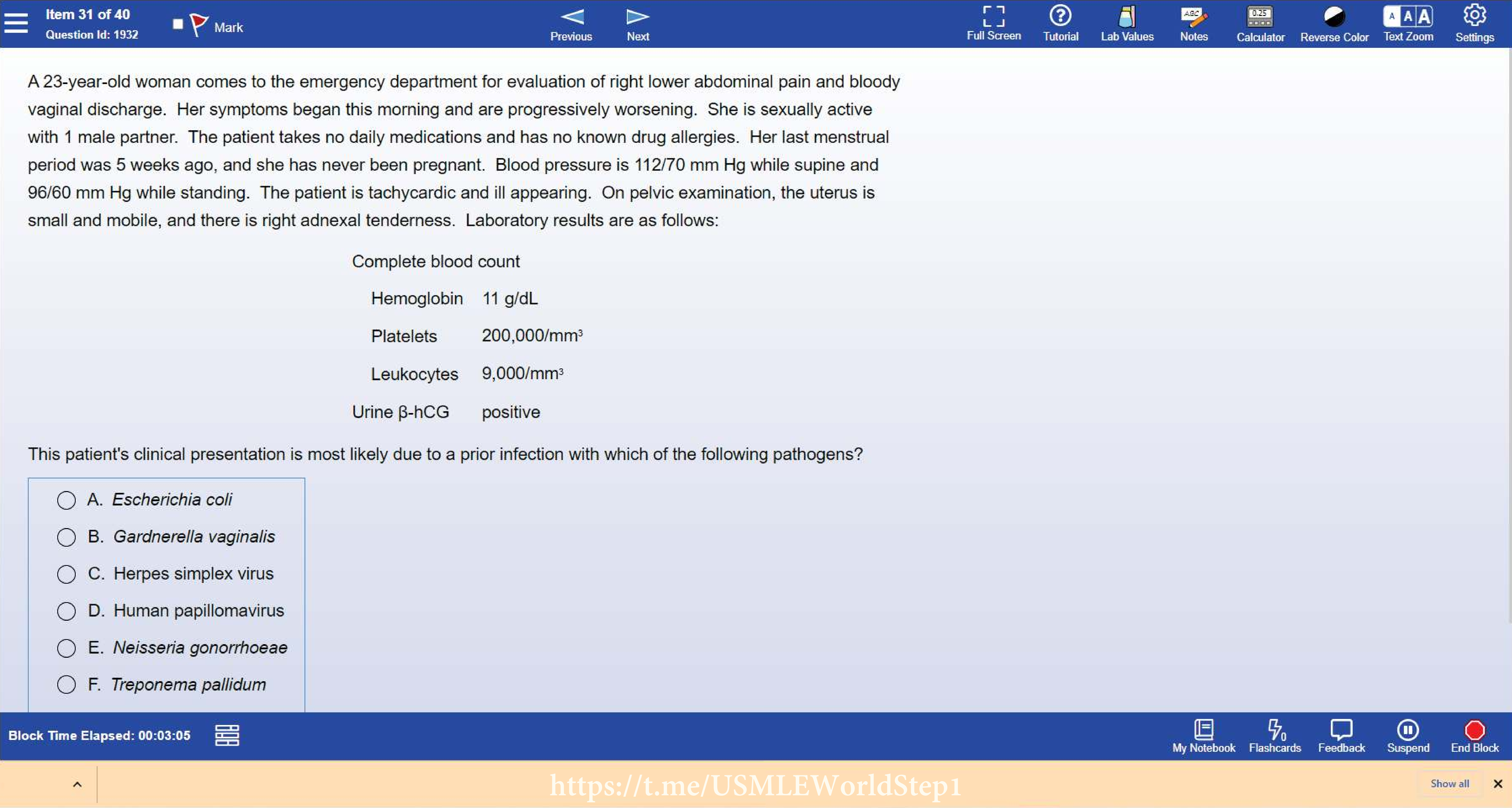
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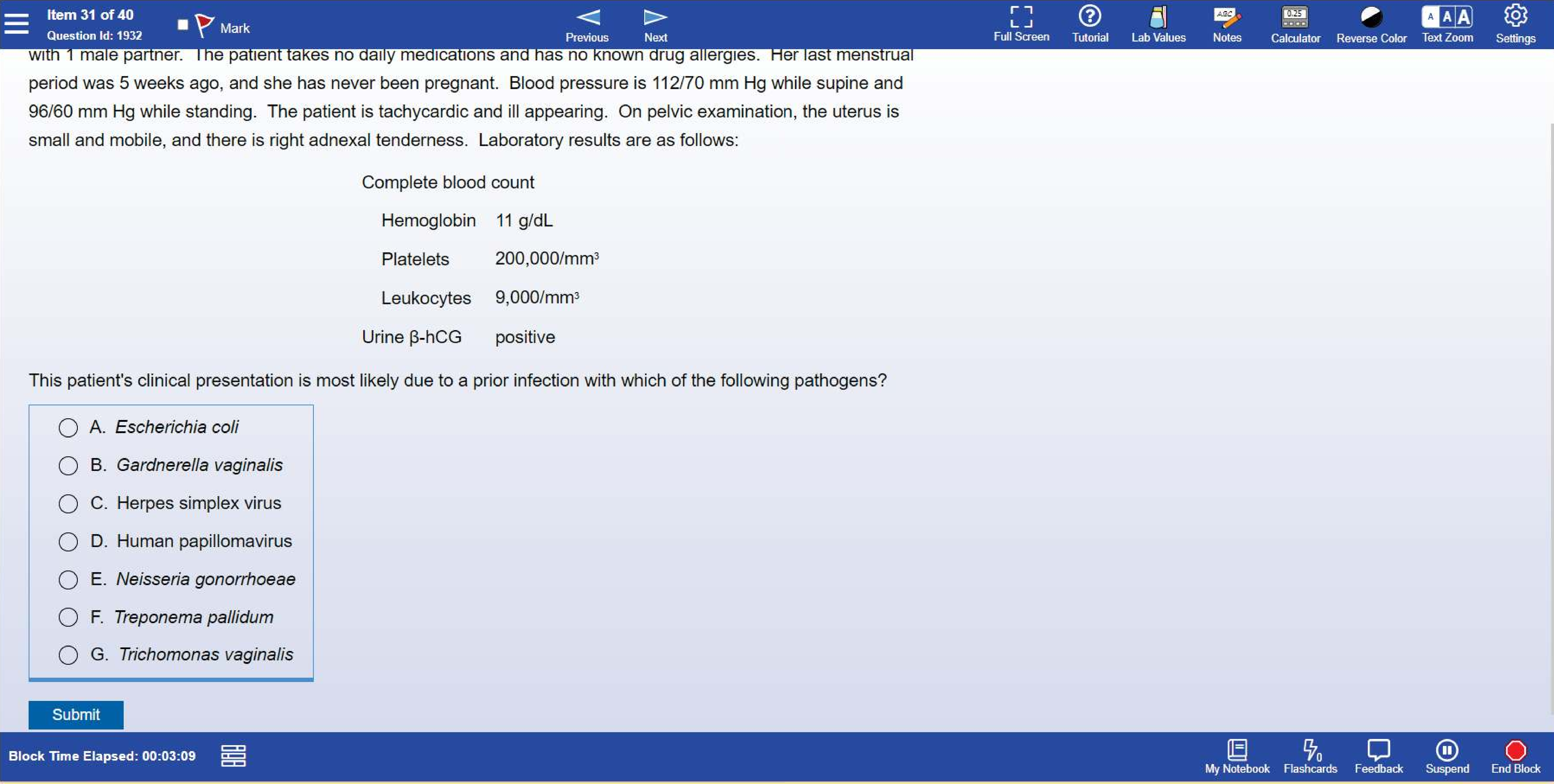
A 23-year-old woman comes to the emergency department for evaluation of right lower abdominal pain and bloody vaginal discharge. Her symptoms began this morning and are progressively worsening. She is sexually active with 1 male partner. The patient takes no daily medications and has no known drug allergies. Her last menstrual period was 5 weeks ago, and she has never been pregnant. Blood pressure is 112/70 mm Hg while supine and 96/60 mm Hg while standing. The patient is tachycardic and ill appearing. On pelvic examination, the uterus is small and mobile, and there is right adnexal tenderness. Laboratory results are as follows:

Complete blood count	
Hemoglobin	11 g/dL
Platelets	200,000/mm^3
Leukocytes	9,000/mm^3
Urine β-hCG	positive

This patient's clinical presentation is most likely due to a prior infection with which of the following pathogens?

○ A. *Escherichia coli*
○ B. *Gardnerella vaginalis*
○ C. Herpes simplex virus
○ D. Human papillomavirus
○ E. *Neisseria gonorrhoeae*
○ F. *Treponema pallidum*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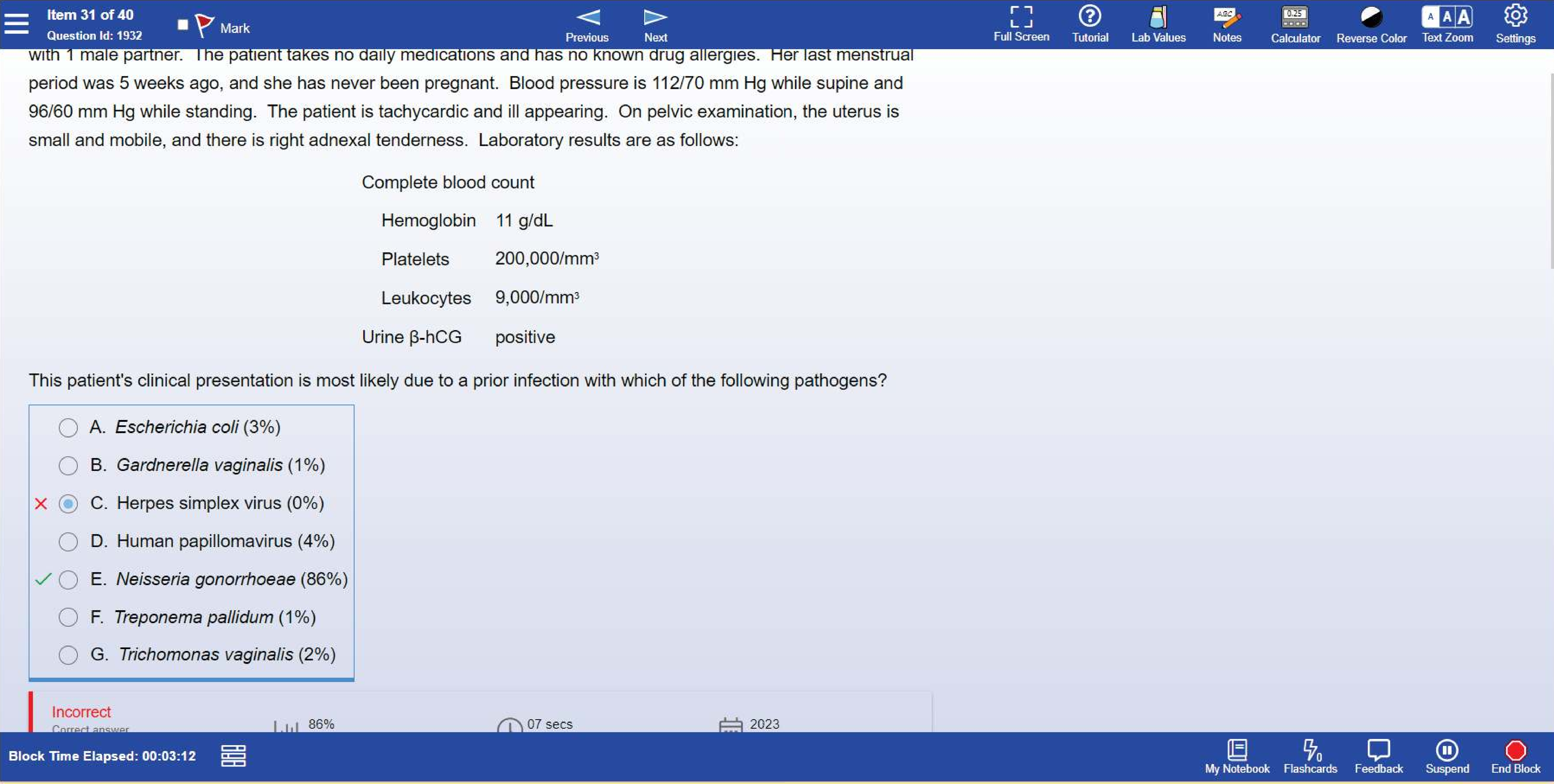
with 1 male partner. The patient takes no daily medications and has no known drug allergies. Her last menstrual period was 5 weeks ago, and she has never been pregnant. Blood pressure is 112/70 mm Hg while supine and 96/60 mm Hg while standing. The patient is tachycardic and ill appearing. On pelvic examination, the uterus is small and mobile, and there is right adnexal tenderness. Laboratory results are as follows:

Complete blood count	
Hemoglobin	11 g/dL
Platelets	200,000/mm^3
Leukocytes	9,000/mm^3
Urine β-hCG	positive

This patient's clinical presentation is most likely due to a prior infection with which of the following pathogens?

○ A. *Escherichia coli*
○ B. *Gardnerella vaginalis*
○ C. Herpes simplex virus
○ D. Human papillomavirus
○ E. *Neisseria gonorrhoeae*
○ F. *Treponema pallidum*
○ G. *Trichomonas vaginalis*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Complete blood count	
Hemoglobin	11 g/dL
Platelets	200,000/mm^3
Leukocytes	9,000/mm^3
Urine β-hCG	positive

This patient's clinical presentation is most likely due to a prior infection with which of the following pathogens?

- ○ A. *Escherichia coli* (3%)
- ○ B. *Gardnerella vaginalis* (1%)
- ✗ ● C. Herpes simplex virus (0%)
- ○ D. Human papillomavirus (4%)
- ✓ ○ E. *Neisseria gonorrhoeae* (86%)
- ○ F. *Treponema pallidum* (1%)
- ○ G. *Trichomonas vaginalis* (2%)

Incorrect
Correct answer

86%

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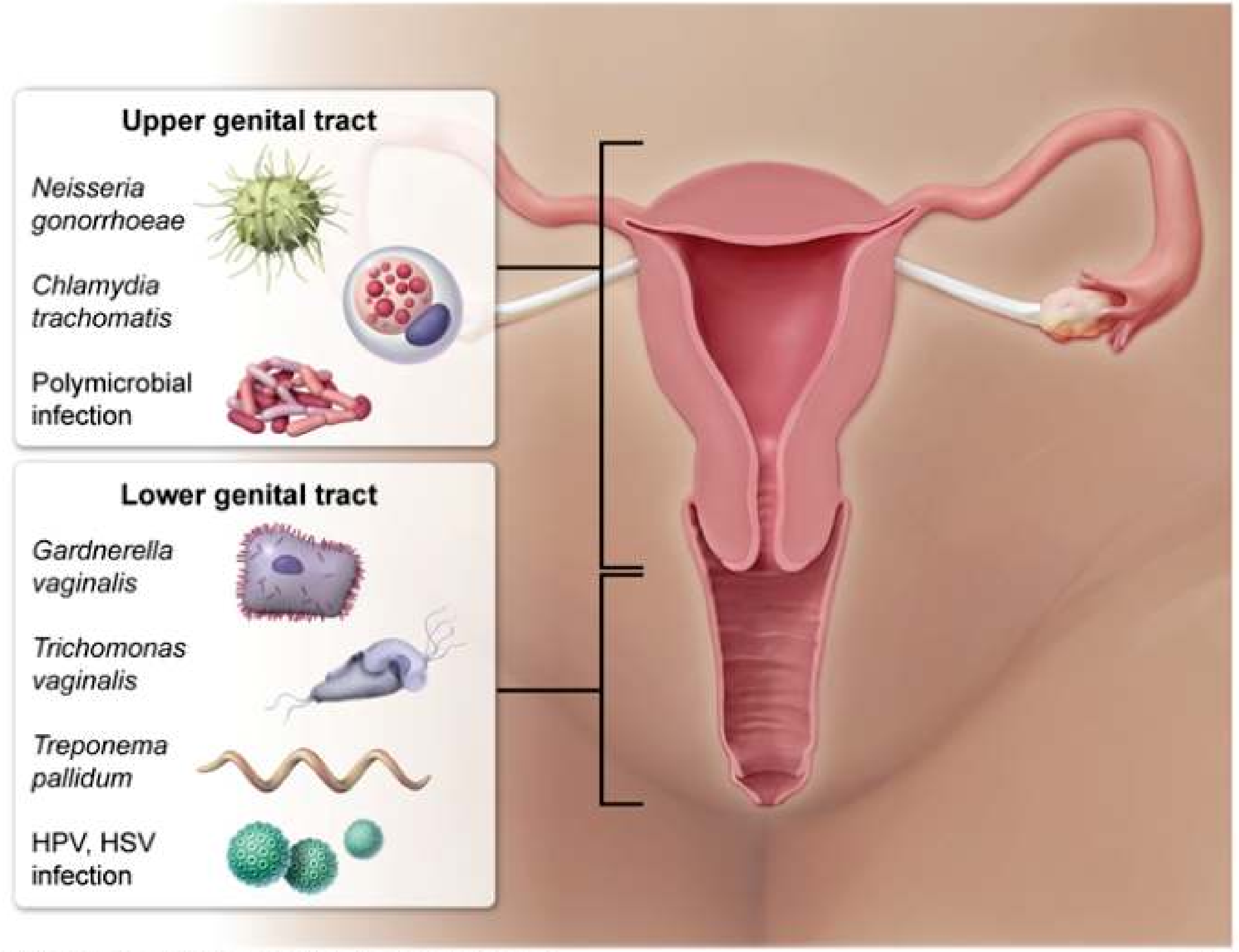
Common pathogens of the female genital tract


Upper genital tract
Neisseria gonorrhoeae
Chlamydia trachomatis
Polymicrobial infection
Lower genital tract
Gardnerella vaginalis
Trichomonas vaginalis
Treponema pallidum
HPV, HSV infection

HPV = human papillomavirus; **HSV** = herpes simplex virus.

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pregnancies occur due to extrauterine pregnancy implantation, typically in the ampulla of the fallopian tube.

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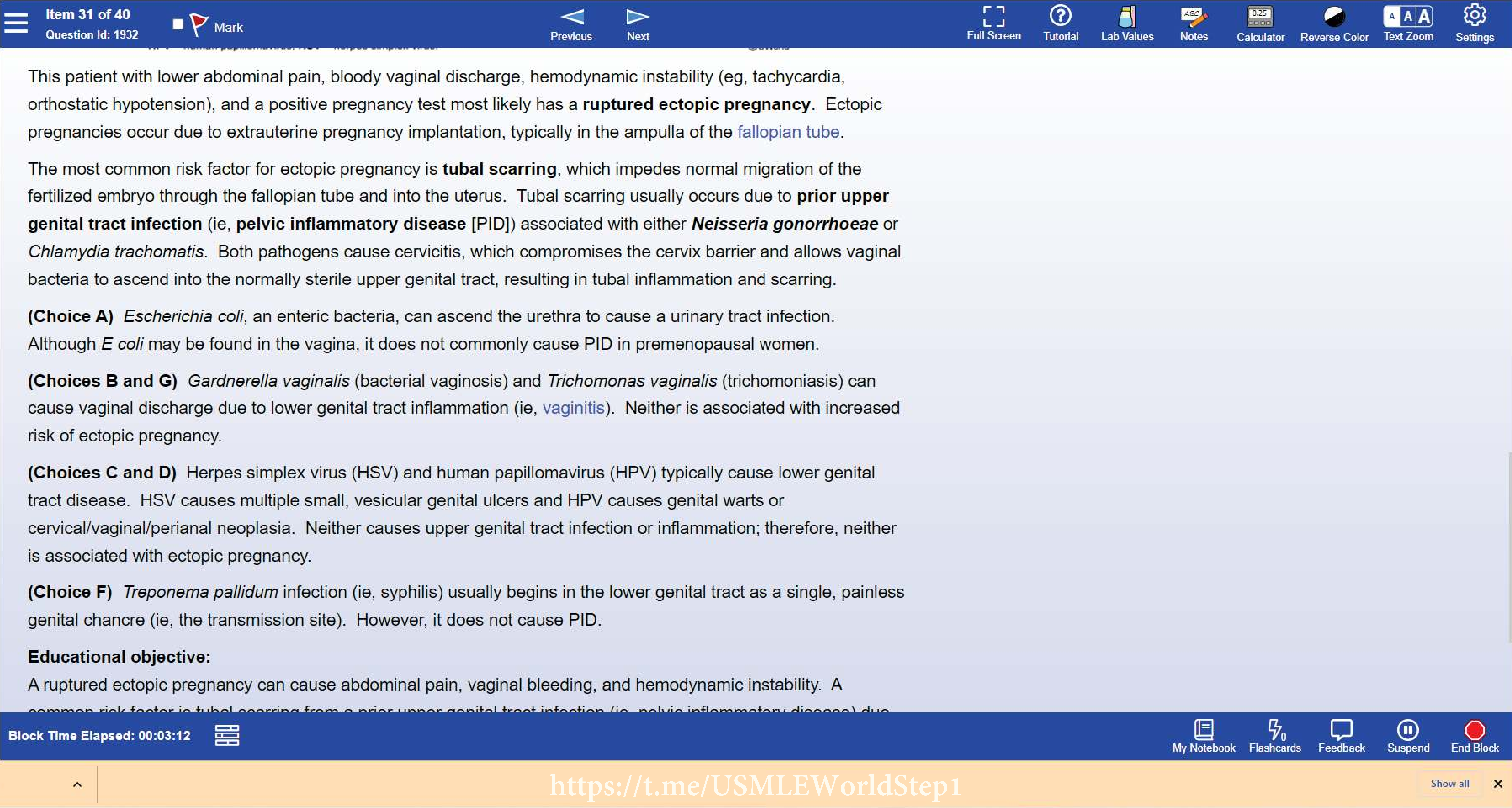


This patient with lower abdominal pain, bloody vaginal discharge, hemodynamic instability (eg, tachycardia, orthostatic hypotension), and a positive pregnancy test most likely has a **ruptured ectopic pregnancy**. Ectopic pregnancies occur due to extrauterine pregnancy implantation, typically in the ampulla of the fallopian tube.

The most common risk factor for ectopic pregnancy is **tubal scarring**, which impedes normal migration of the fertilized embryo through the fallopian tube and into the uterus. Tubal scarring usually occurs due to **prior upper genital tract infection** (ie, **pelvic inflammatory disease** [PID]) associated with either ***Neisseria gonorrhoeae*** or *Chlamydia trachomatis*. Both pathogens cause cervicitis, which compromises the cervix barrier and allows vaginal bacteria to ascend into the normally sterile upper genital tract, resulting in tubal inflammation and scarring.

(Choice A) *Escherichia coli*, an enteric bacteria, can ascend the urethra to cause a urinary tract infection. Although *E coli* may be found in the vagina, it does not commonly cause PID in premenopausal women.

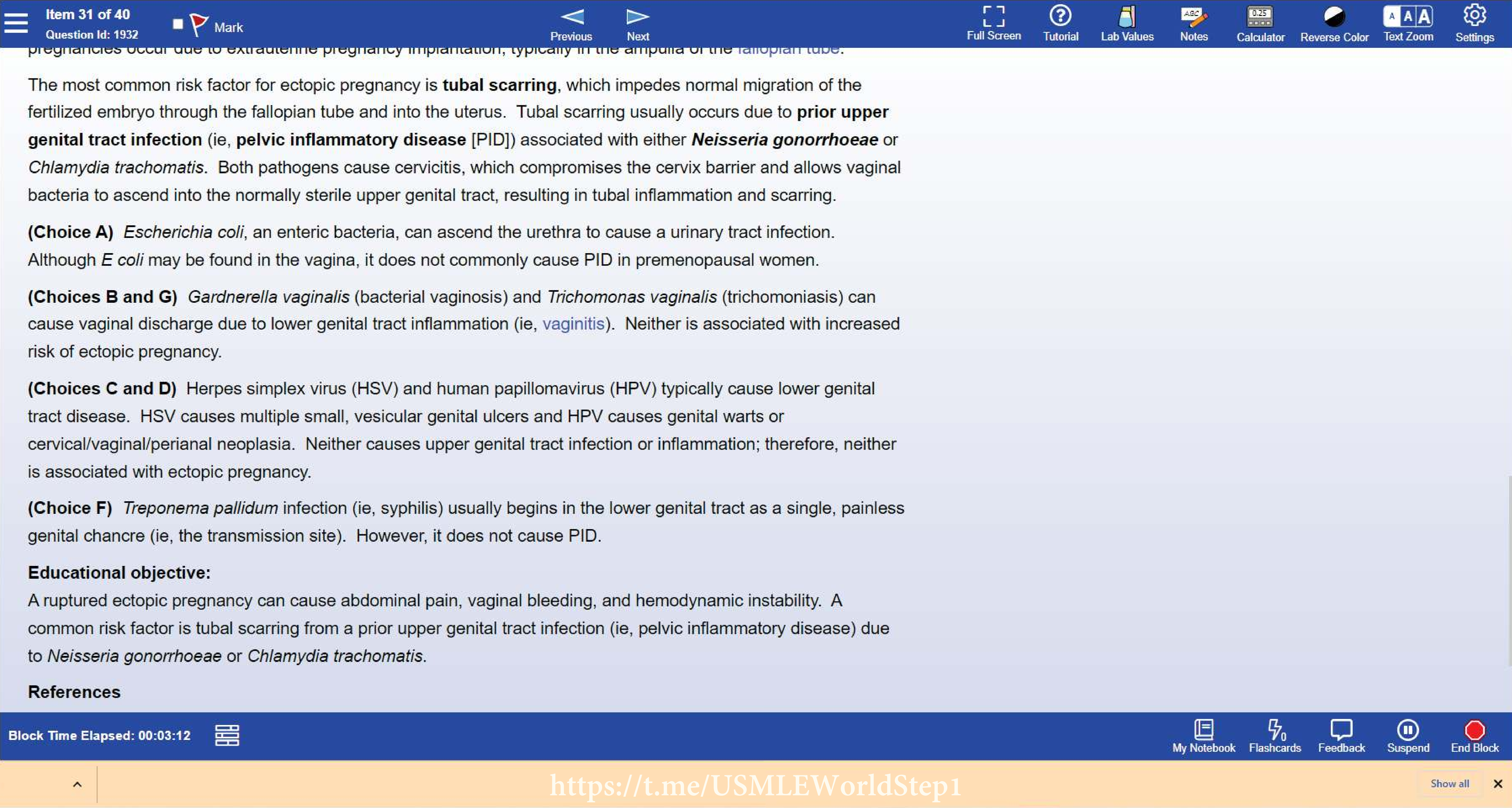
(Choices B and G) *Gardnerella vaginalis* (bacterial vaginosis) and *Trichomonas vaginalis* (trichomoniasis) can cause vaginal discharge due to lower genital tract inflammation (ie, vaginitis). Neither is associated with increased risk of ectopic pregnancy.

(Choices C and D) Herpes simplex virus (HSV) and human papillomavirus (HPV) typically cause lower genital tract disease. HSV causes multiple small, vesicular genital ulcers and HPV causes genital warts or cervical/vaginal/perianal neoplasia. Neither causes upper genital tract infection or inflammation; therefore, neither is associated with ectopic pregnancy.

(Choice F) *Treponema pallidum* infection (ie, syphilis) usually begins in the lower genital tract as a single, painless genital chancre (ie, the transmission site). However, it does not cause PID.

Educational objective:

A ruptured ectopic pregnancy can cause abdominal pain, vaginal bleeding, and hemodynamic instability. A



pregnancies occur due to extrauterine pregnancy implantation, typically in the ampulla of the fallopian tube.

The most common risk factor for ectopic pregnancy is **tubal scarring**, which impedes normal migration of the fertilized embryo through the fallopian tube and into the uterus. Tubal scarring usually occurs due to **prior upper genital tract infection** (ie, **pelvic inflammatory disease** [PID]) associated with either ***Neisseria gonorrhoeae*** or *Chlamydia trachomatis*. Both pathogens cause cervicitis, which compromises the cervix barrier and allows vaginal bacteria to ascend into the normally sterile upper genital tract, resulting in tubal inflammation and scarring.

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(Choices B and G) *Gardnerella vaginalis* (bacterial vaginosis) and *Trichomonas vaginalis* (trichomoniasis) can cause vaginal discharge due to lower genital tract inflammation (ie, vaginitis). Neither is associated with increased risk of ectopic pregnancy.

(Choices C and D) Herpes simplex virus (HSV) and human papillomavirus (HPV) typically cause lower genital tract disease. HSV causes multiple small, vesicular genital ulcers and HPV causes genital warts or cervical/vaginal/perianal neoplasia. Neither causes upper genital tract infection or inflammation; therefore, neither is associated with ectopic pregnancy.

(Choice F) *Treponema pallidum* infection (ie, syphilis) usually begins in the lower genital tract as a single, painless genital chancre (ie, the transmission site). However, it does not cause PID.

Educational objective:
A ruptured ectopic pregnancy can cause abdominal pain, vaginal bleeding, and hemodynamic instability. A common risk factor is tubal scarring from a prior upper genital tract infection (ie, pelvic inflammatory disease) due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

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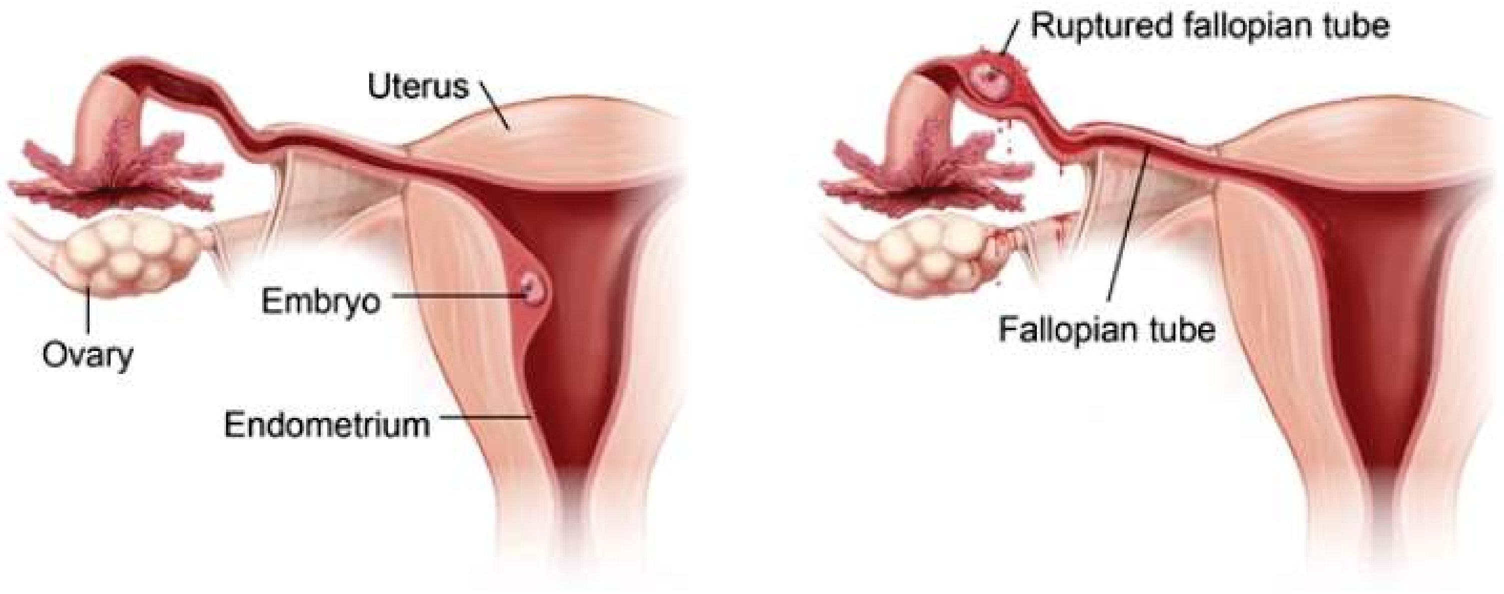
Ruptured ectopic pregnancy



Uterus
Embryo
Ovary
Endometrium
Ruptured fallopian tube
Fallopian tube

Normal pregnancy **Ectopic pregnancy**

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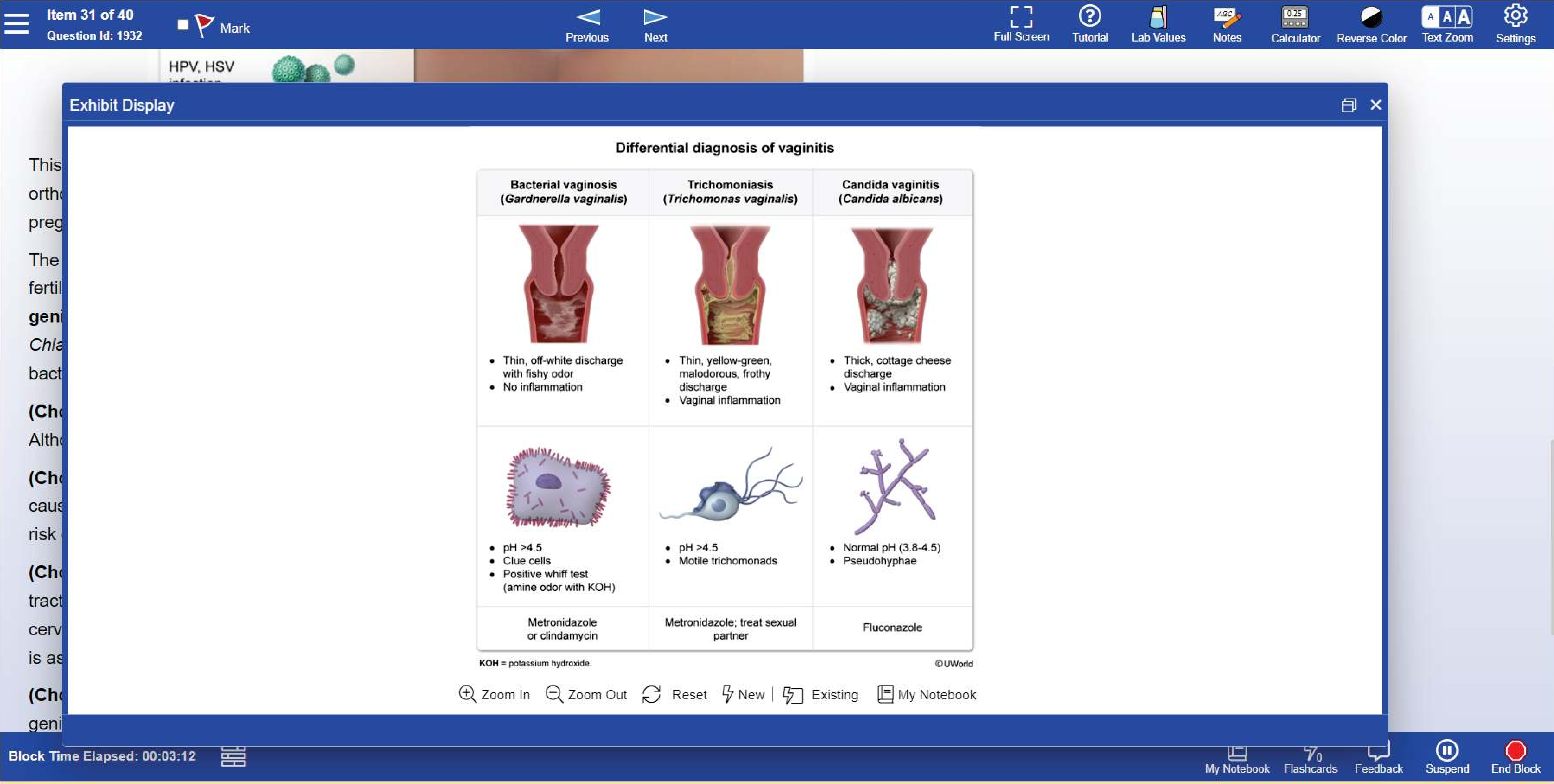
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Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	Trichomoniasis (*Trichomonas vaginalis*)	Candida vaginitis (*Candida albicans*)
• Thin, off-white discharge with fishy odor • No inflammation	• Thin, yellow-green, malodorous, frothy discharge • Vaginal inflammation	• Thick, cottage cheese discharge • Vaginal inflammation
• pH >4.5 • Clue cells • Positive whiff test (amine odor with KOH)	• pH >4.5 • Motile trichomonads	• Normal pH (3.8-4.5) • Pseudohyphae
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

KOH = potassium hydroxide.

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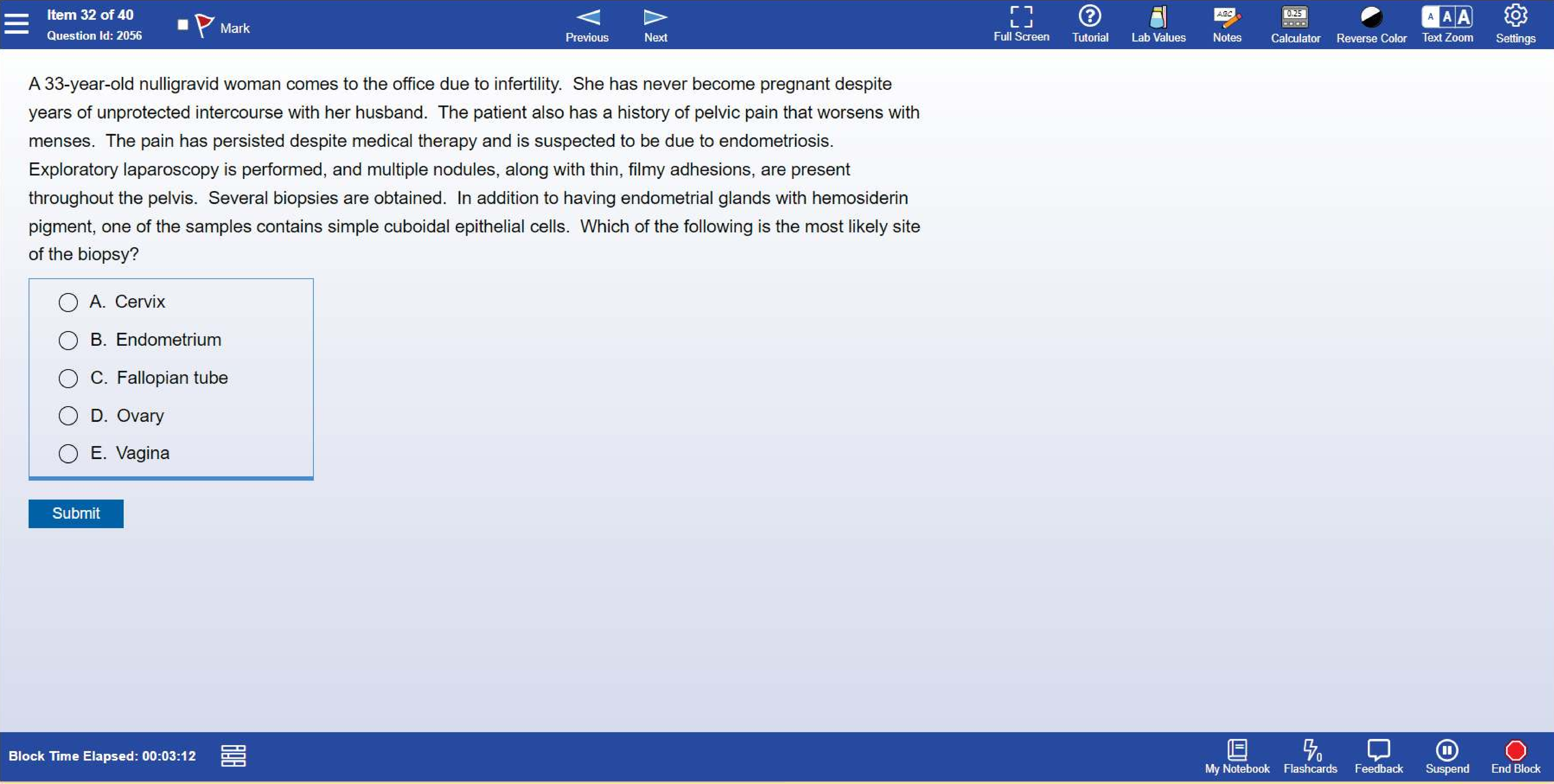
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A 33-year-old nulligravid woman comes to the office due to infertility. She has never become pregnant despite years of unprotected intercourse with her husband. The patient also has a history of pelvic pain that worsens with menses. The pain has persisted despite medical therapy and is suspected to be due to endometriosis. Exploratory laparoscopy is performed, and multiple nodules, along with thin, filmy adhesions, are present throughout the pelvis. Several biopsies are obtained. In addition to having endometrial glands with hemosiderin pigment, one of the samples contains simple cuboidal epithelial cells. Which of the following is the most likely site of the biopsy?

- ○ A. Cervix
- ○ B. Endometrium
- ○ C. Fallopian tube
- ○ D. Ovary
- ○ E. Vagina

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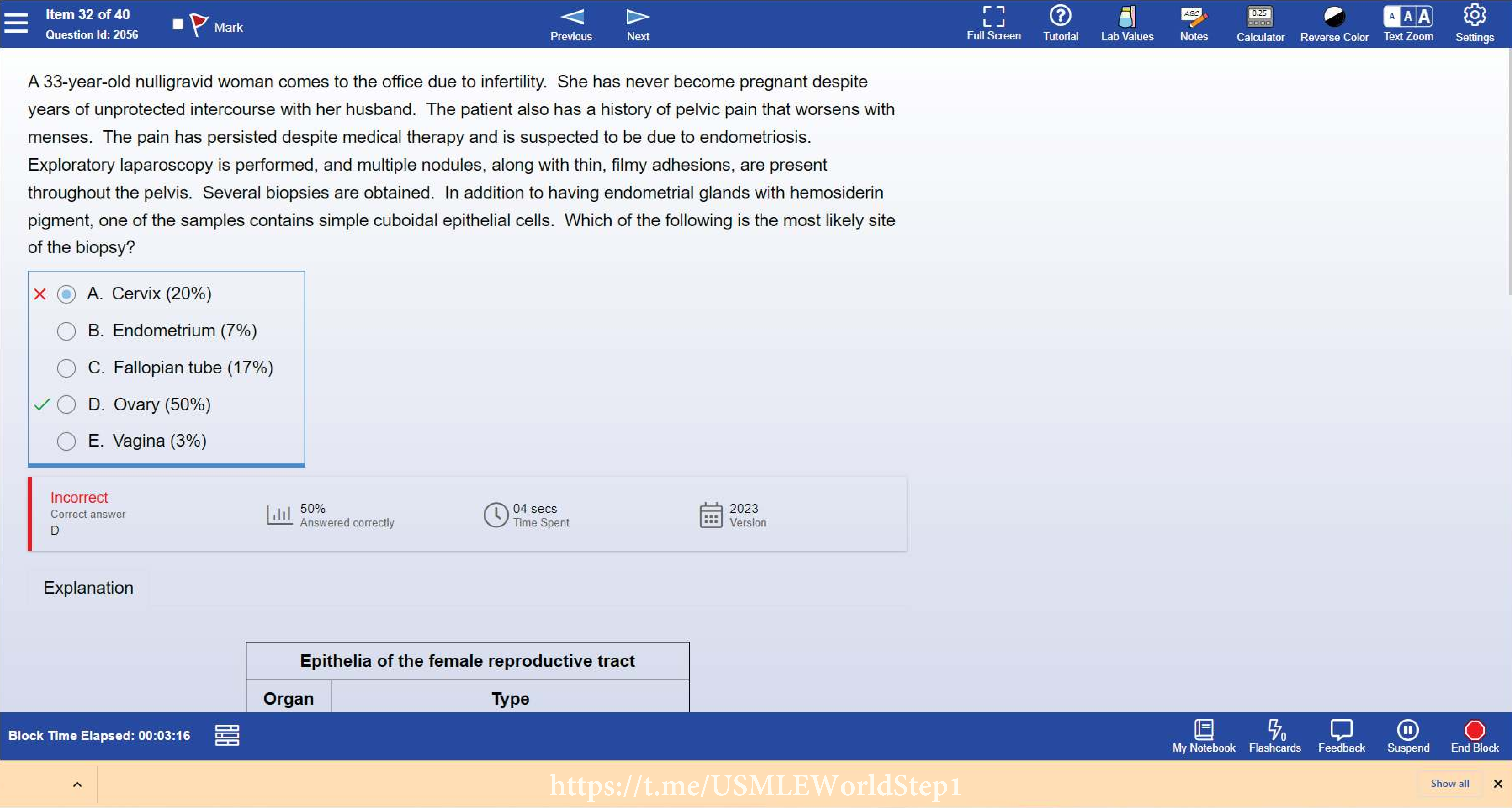
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✗ ● A. Cervix (20%)
○ B. Endometrium (7%)
○ C. Fallopian tube (17%)
✓ ○ D. Ovary (50%)
○ E. Vagina (3%)

Incorrect
Correct answer
D

50%
Answered correctly

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Explanation

Epithelia of the female reproductive tract	
Organ	**Type**

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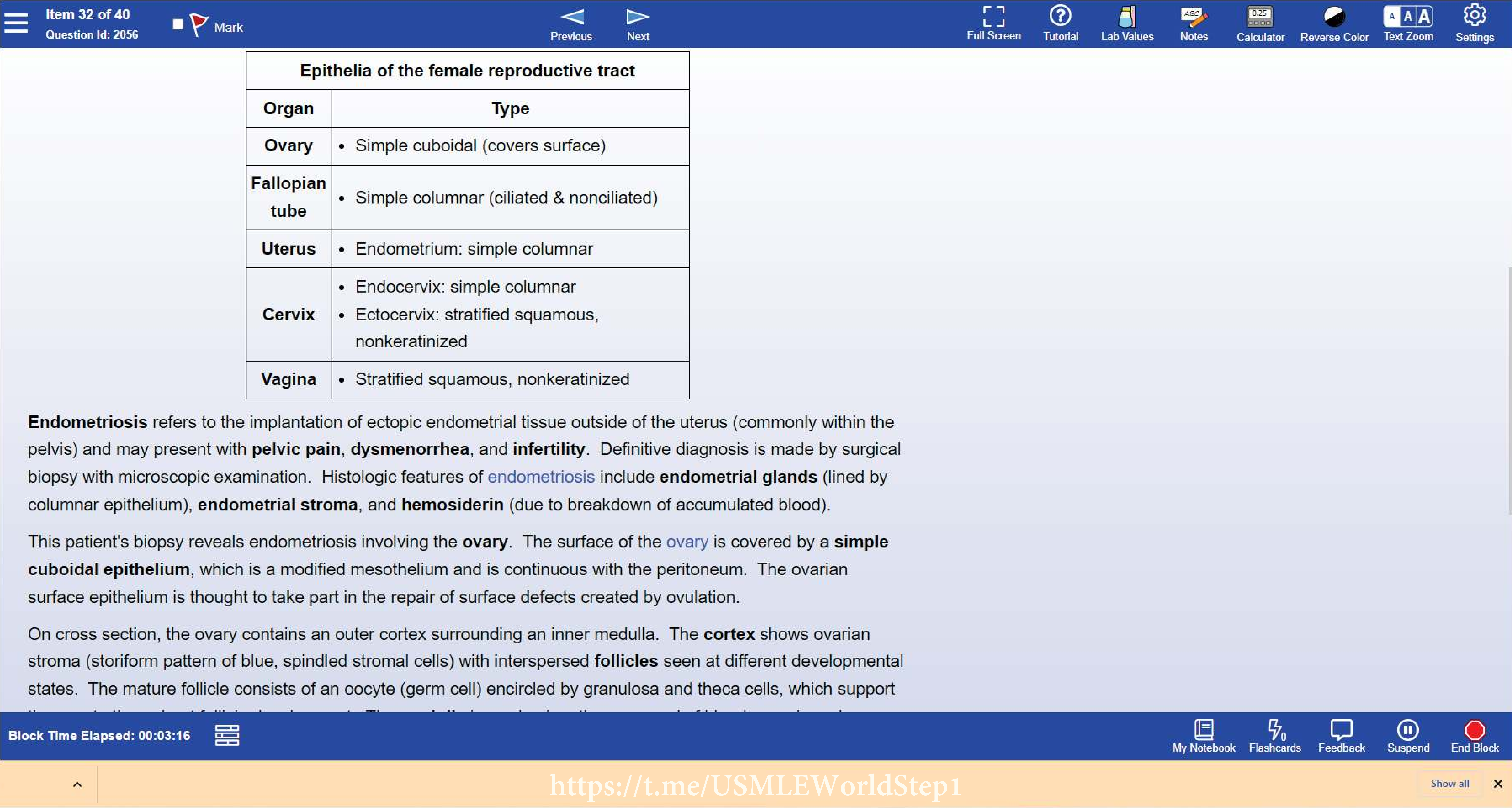
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Epithelia of the female reproductive tract	
Organ	**Type**
Ovary	• Simple cuboidal (covers surface)
Fallopian tube	• Simple columnar (ciliated & nonciliated)
Uterus	• Endometrium: simple columnar
Cervix	• Endocervix: simple columnar • Ectocervix: stratified squamous, nonkeratinized
Vagina	• Stratified squamous, nonkeratinized

Endometriosis refers to the implantation of ectopic endometrial tissue outside of the uterus (commonly within the pelvis) and may present with **pelvic pain**, **dysmenorrhea**, and **infertility**. Definitive diagnosis is made by surgical biopsy with microscopic examination. Histologic features of endometriosis include **endometrial glands** (lined by columnar epithelium), **endometrial stroma**, and **hemosiderin** (due to breakdown of accumulated blood).

This patient's biopsy reveals endometriosis involving the **ovary**. The surface of the ovary is covered by a **simple cuboidal epithelium**, which is a modified mesothelium and is continuous with the peritoneum. The ovarian surface epithelium is thought to take part in the repair of surface defects created by ovulation.

On cross section, the ovary contains an outer cortex surrounding an inner medulla. The **cortex** shows ovarian stroma (storiform pattern of blue, spindled stromal cells) with interspersed **follicles** seen at different developmental states. The mature follicle consists of an oocyte (germ cell) encircled by granulosa and theca cells, which support

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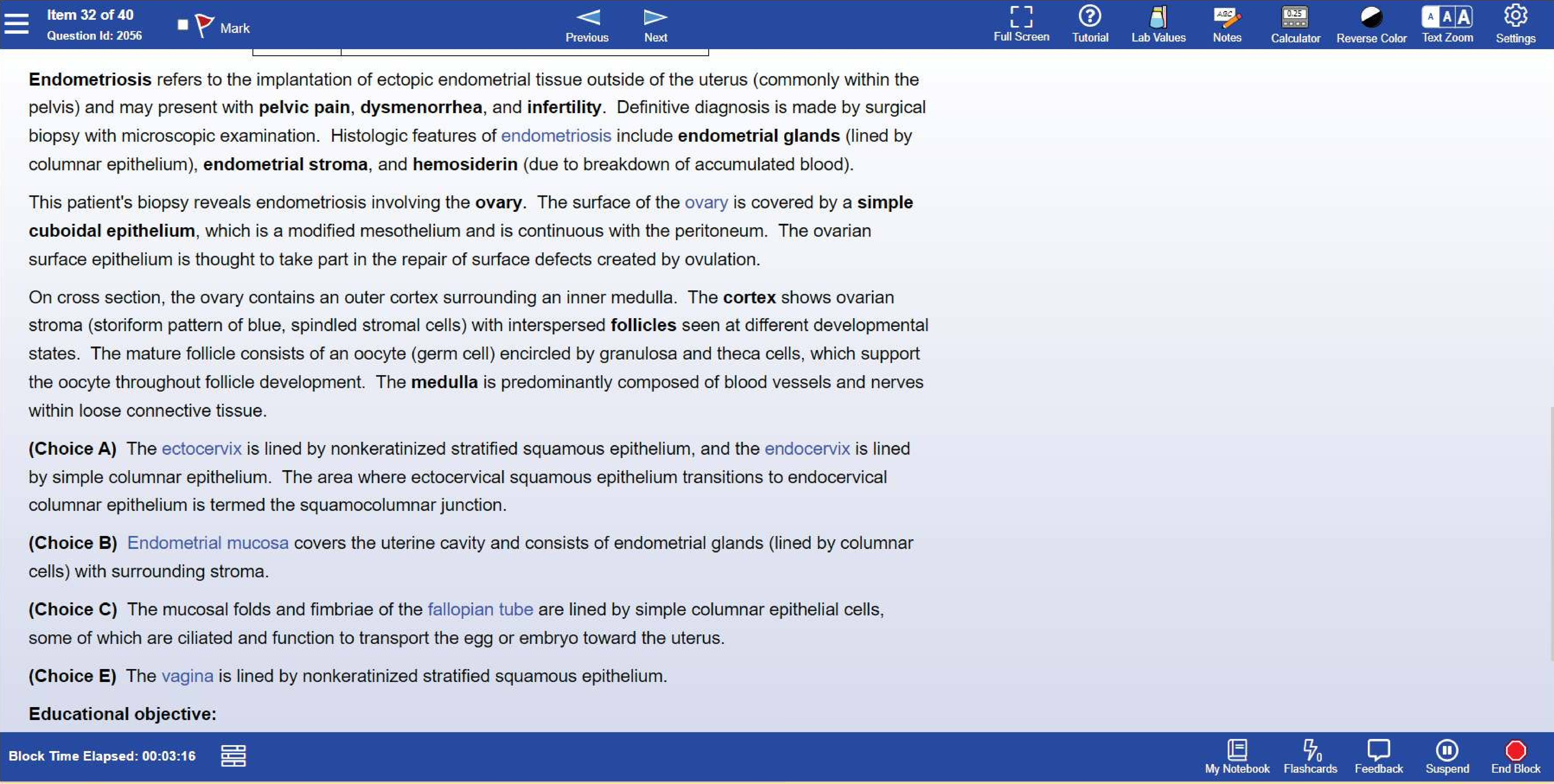

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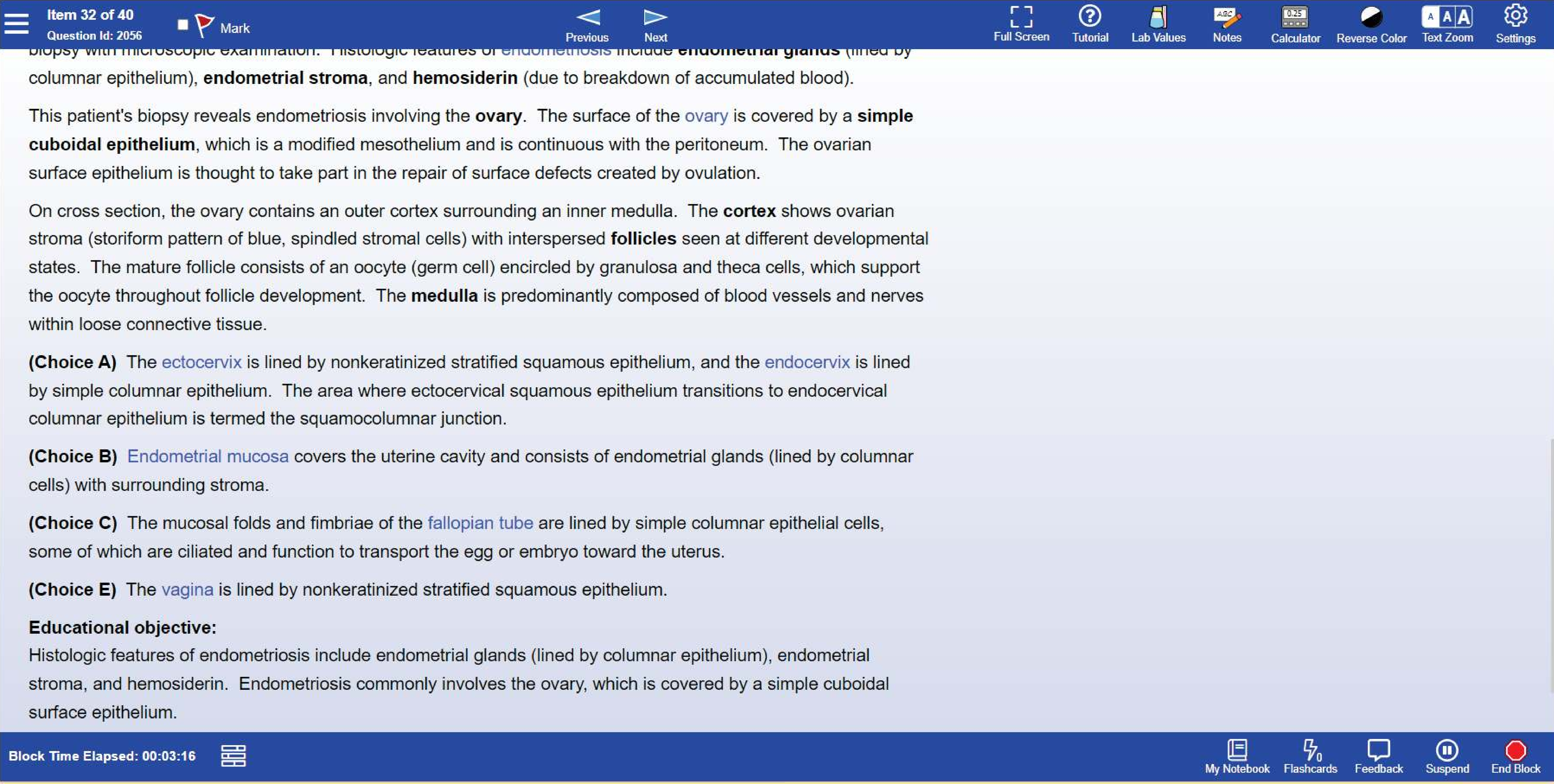
(Choice A) The ectocervix is lined by nonkeratinized stratified squamous epithelium, and the endocervix is lined by simple columnar epithelium. The area where ectocervical squamous epithelium transitions to endocervical columnar epithelium is termed the squamocolumnar junction.

(Choice B) Endometrial mucosa covers the uterine cavity and consists of endometrial glands (lined by columnar cells) with surrounding stroma.

(Choice C) The mucosal folds and fimbriae of the fallopian tube are lined by simple columnar epithelial cells, some of which are ciliated and function to transport the egg or embryo toward the uterus.

(Choice E) The vagina is lined by nonkeratinized stratified squamous epithelium.

Educational objective:



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(Choice E) The vagina is lined by nonkeratinized stratified squamous epithelium.

Educational objective:
Histologic features of endometriosis include endometrial glands (lined by columnar epithelium), endometrial stroma, and hemosiderin. Endometriosis commonly involves the ovary, which is covered by a simple cuboidal surface epithelium.

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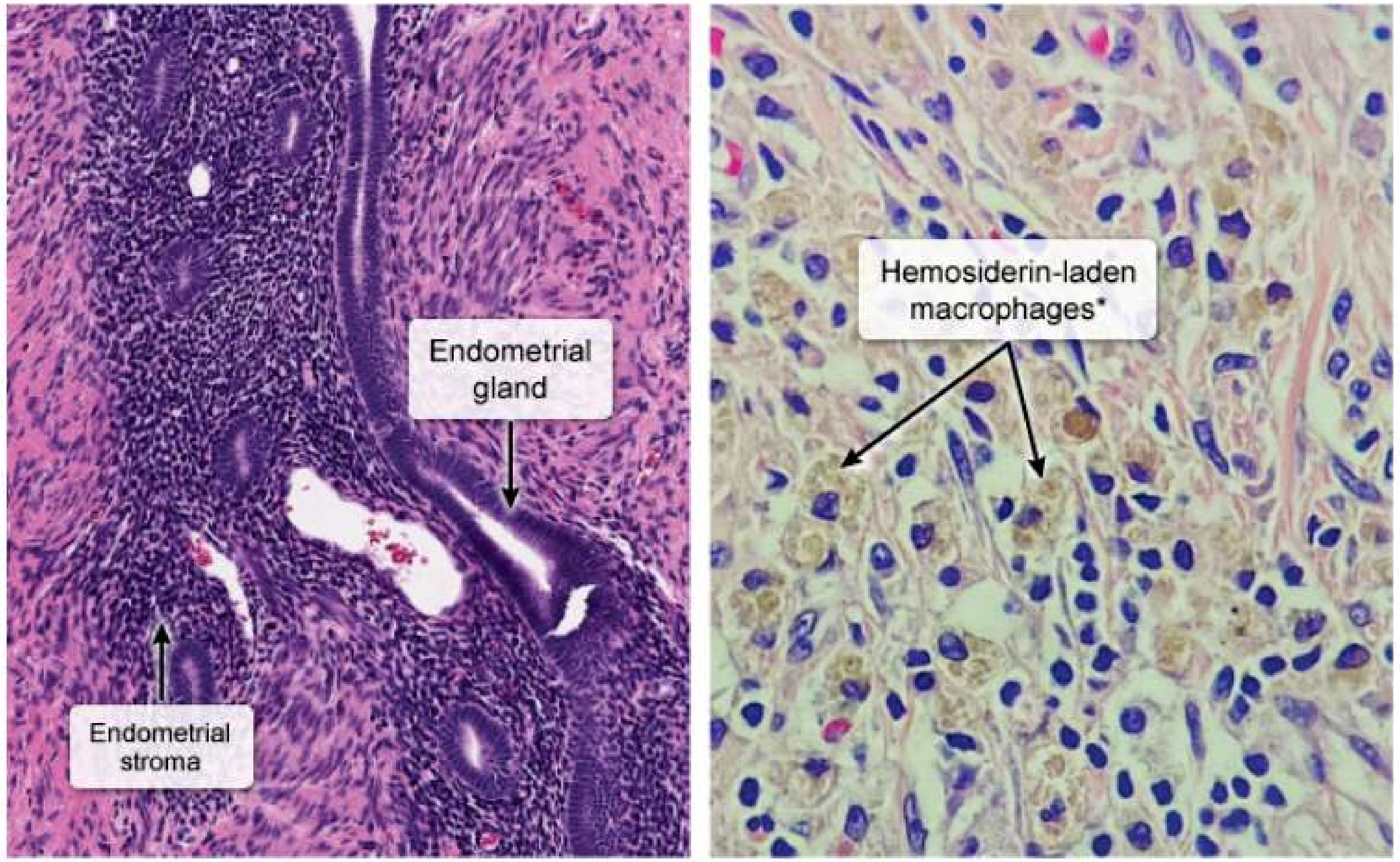
Uterus	• Endometrium: simple columnar

Exhibit Display

Endometriosis


Endometrial gland
Endometrial stroma
Hemosiderin-laden macrophages*

*Indicate prior hemorrhage

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(Choice B) Endometrial mucosa covers the uterine cavity and consists of endometrial glands (lined by columnar

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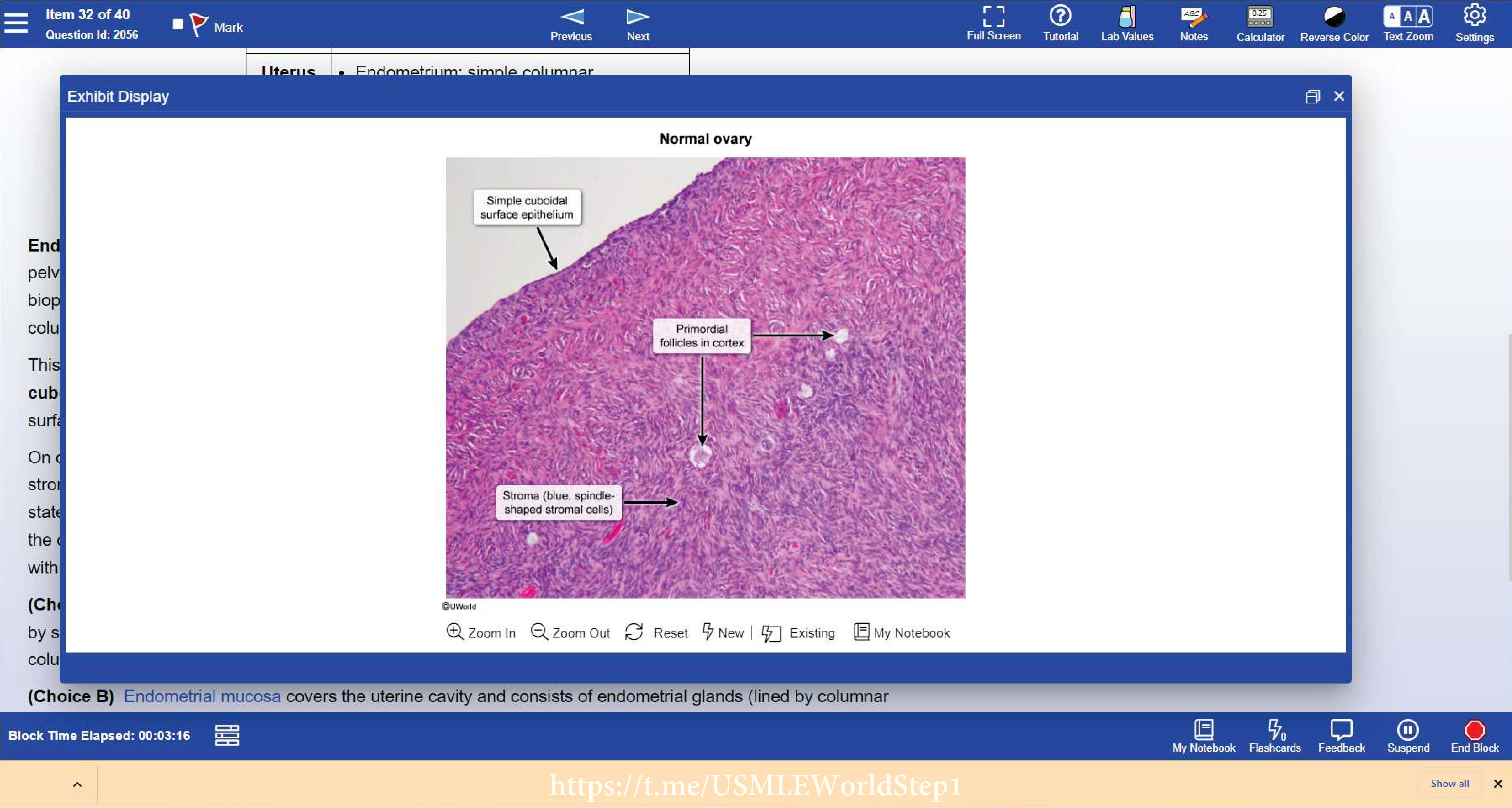
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Exhibit Display
Simple cuboidal surface epithelium
Primordial follicles in cortex
Stroma (blue, spindle-shaped stromal cells)
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Uterus	• Endometrium: simple columnar

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Normal ovary

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(Choice B) Endometrial mucosa covers the uterine cavity and consists of endometrial glands (lined by columnar

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Cervix	• Ectocervix: stratified squamous,

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some of which are ciliated and function to transport the egg or embryo toward the uterus.

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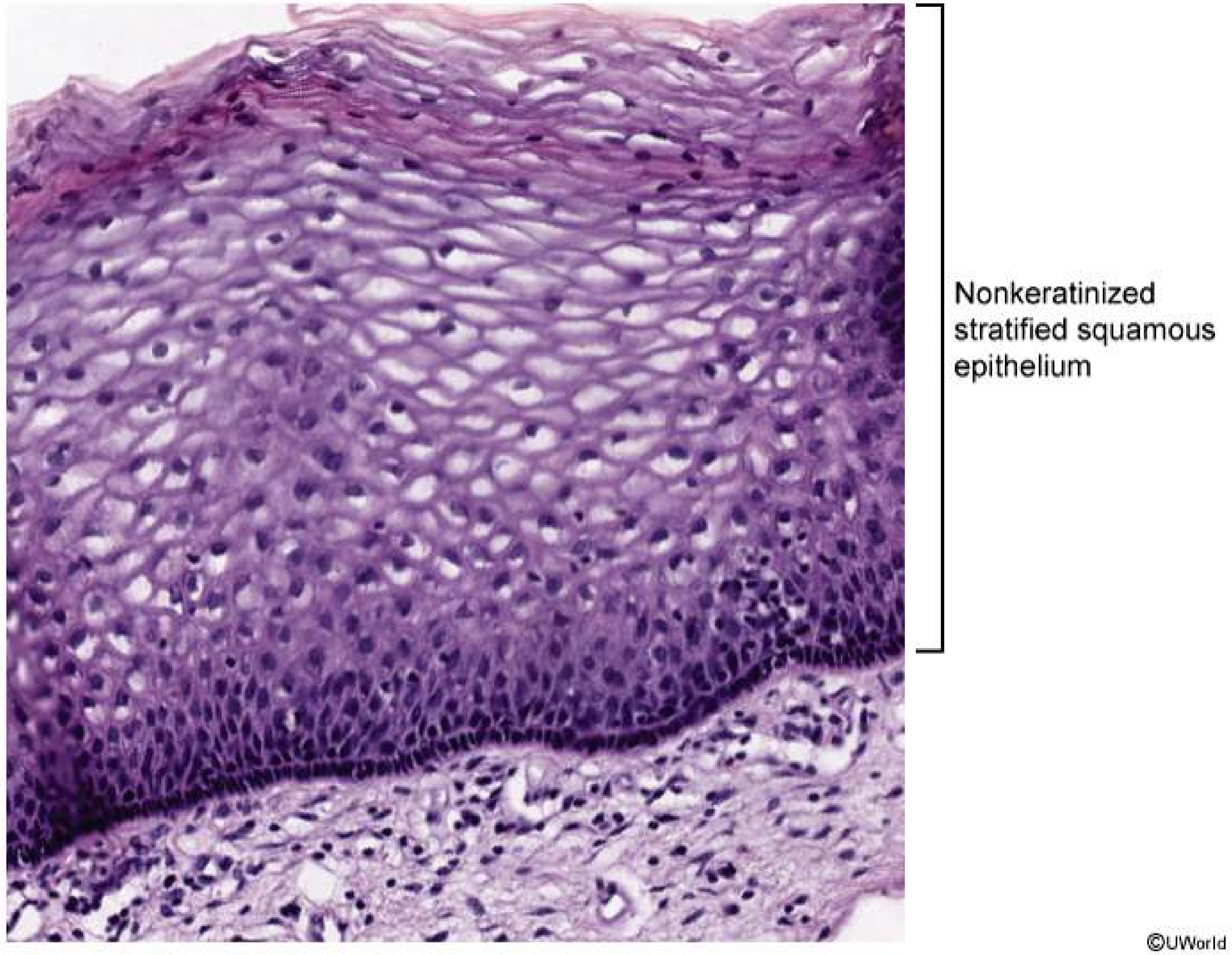
Normal ectocervix


Nonkeratinized stratified squamous epithelium
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Cervix	- Ectocervix: stratified squamous,

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some of which are ciliated and function to transport the egg or embryo toward the uterus.

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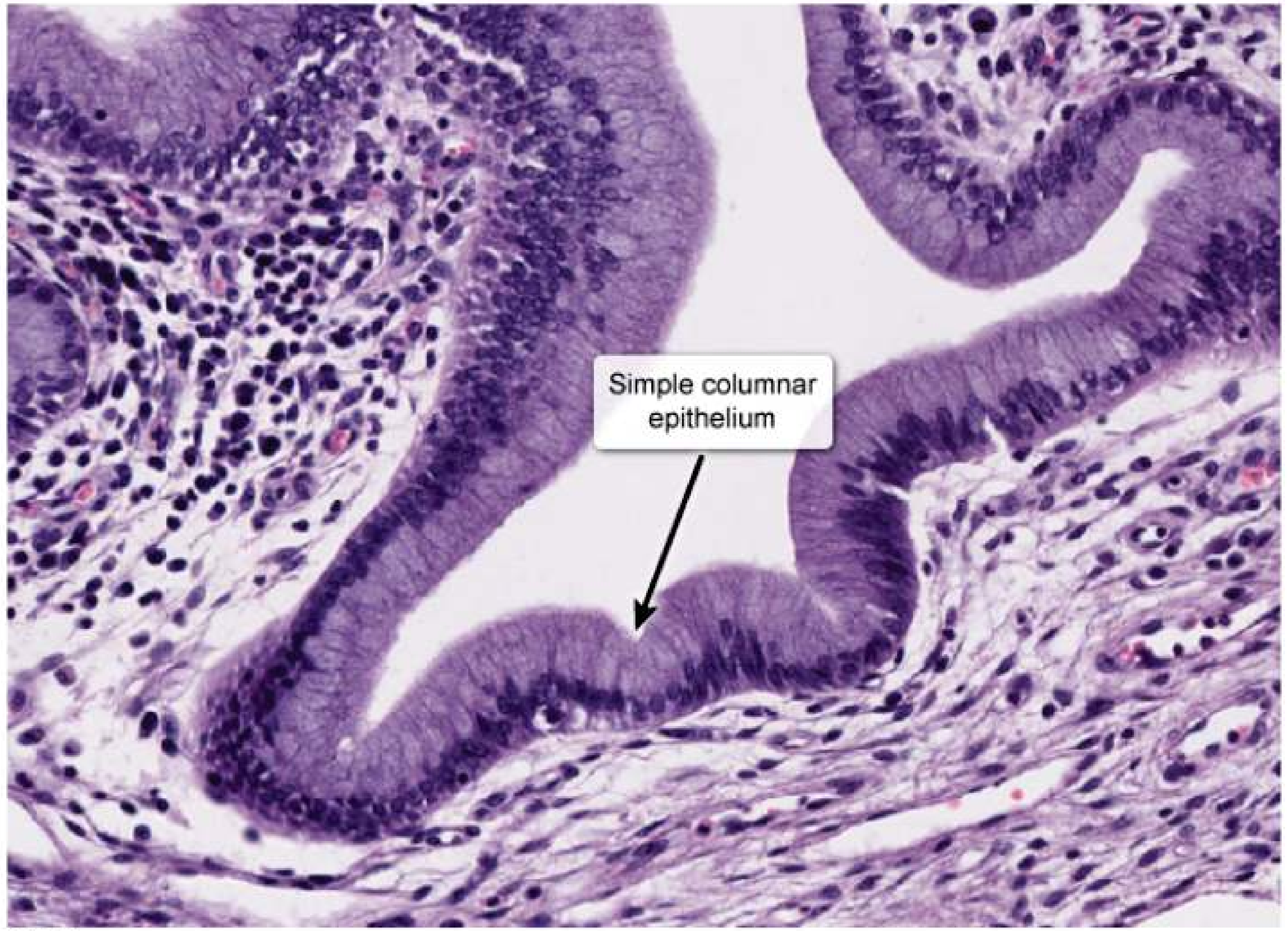
Normal endocervix



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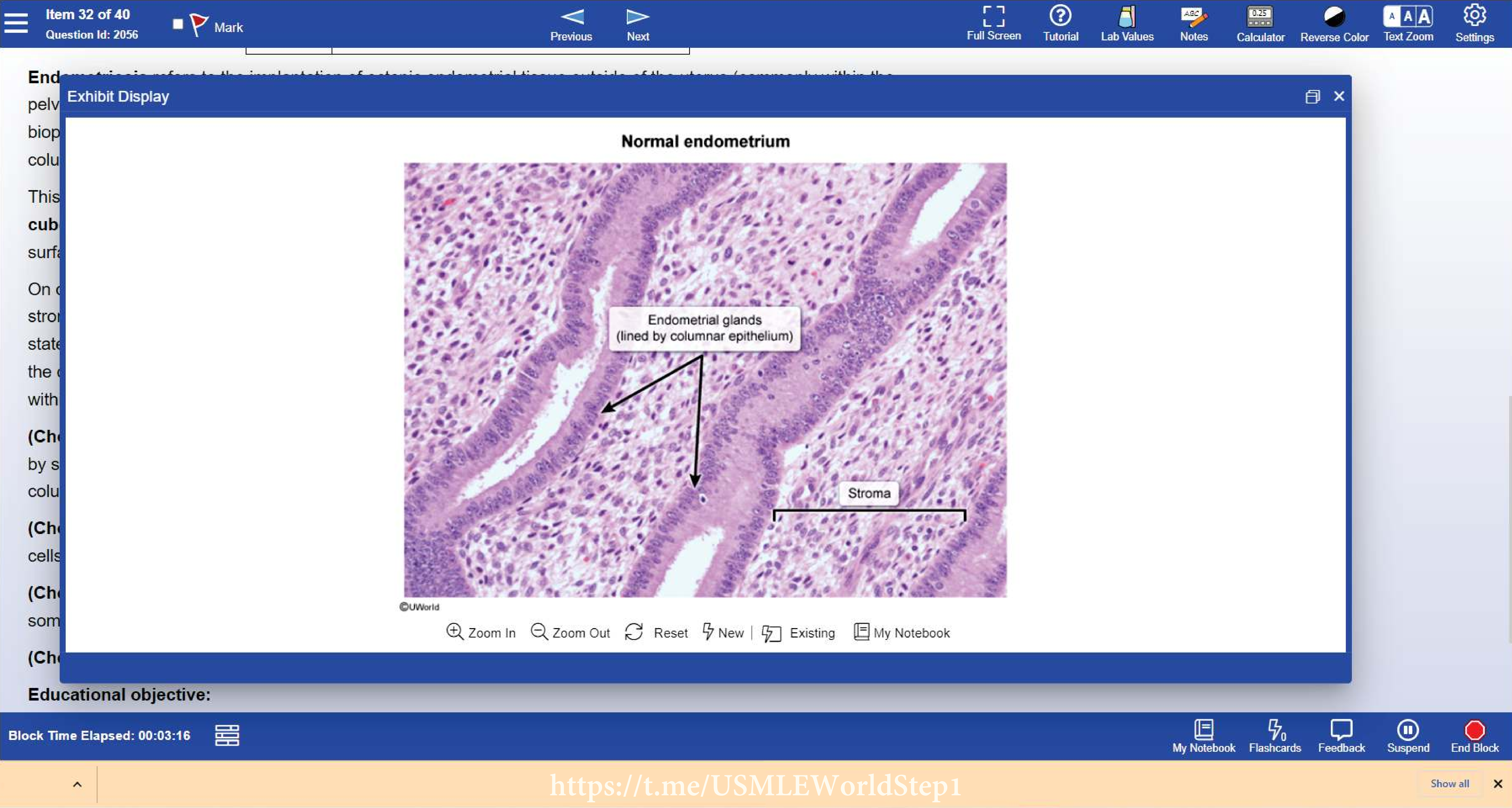

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Educational objective:

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Normal endometrium

Endometrial glands
(lined by columnar epithelium)
Stroma
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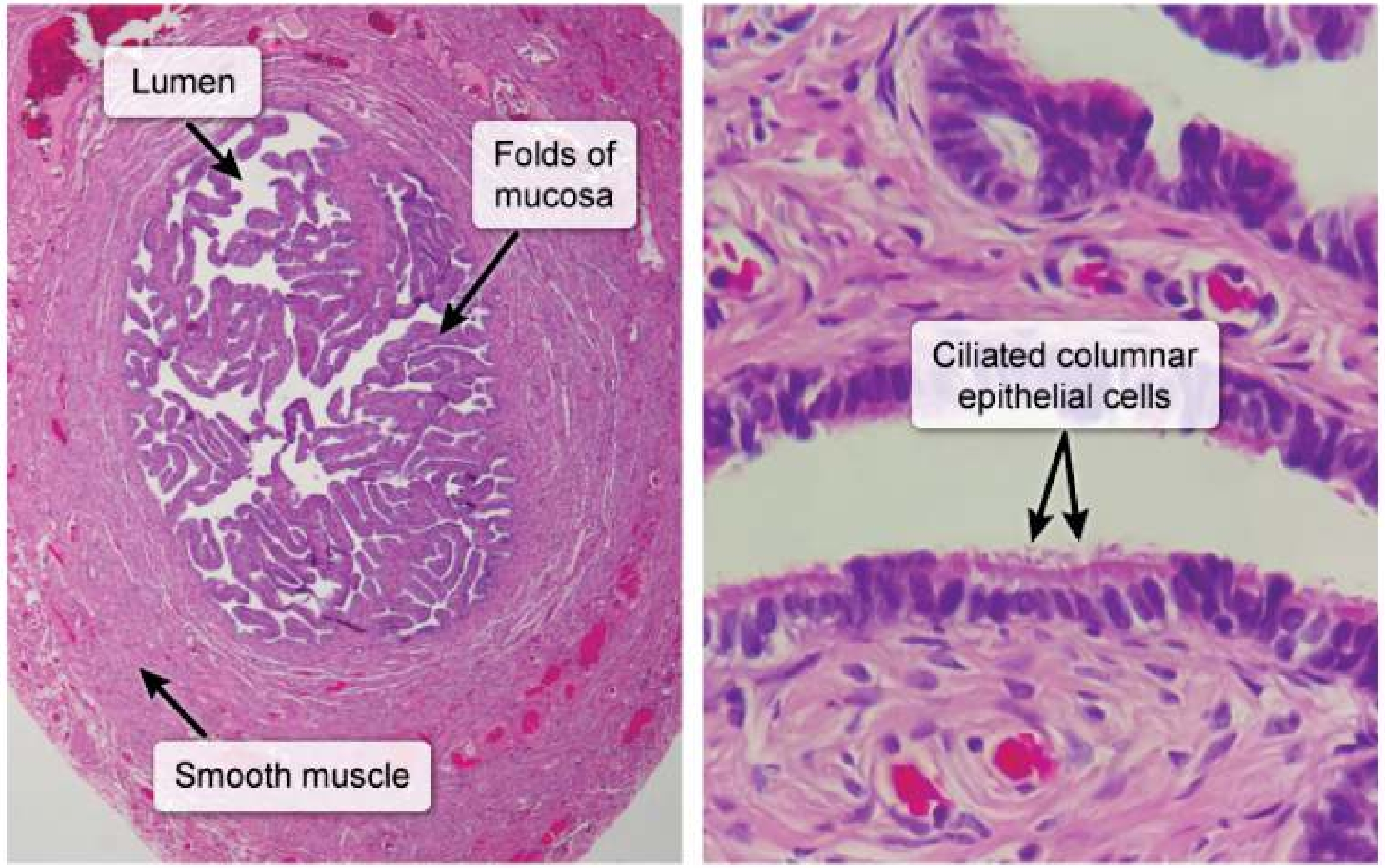
Fallopian tube


Lumen
Folds of mucosa
Smooth muscle
Ciliated columnar epithelial cells

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Educational objective:

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biopsy with microscopic examination. Histologic features of endometriosis include **endometrial glands** (lined by columnar epithelium), **endometrial stroma**, and **hemosiderin** (due to breakdown of accumulated blood).

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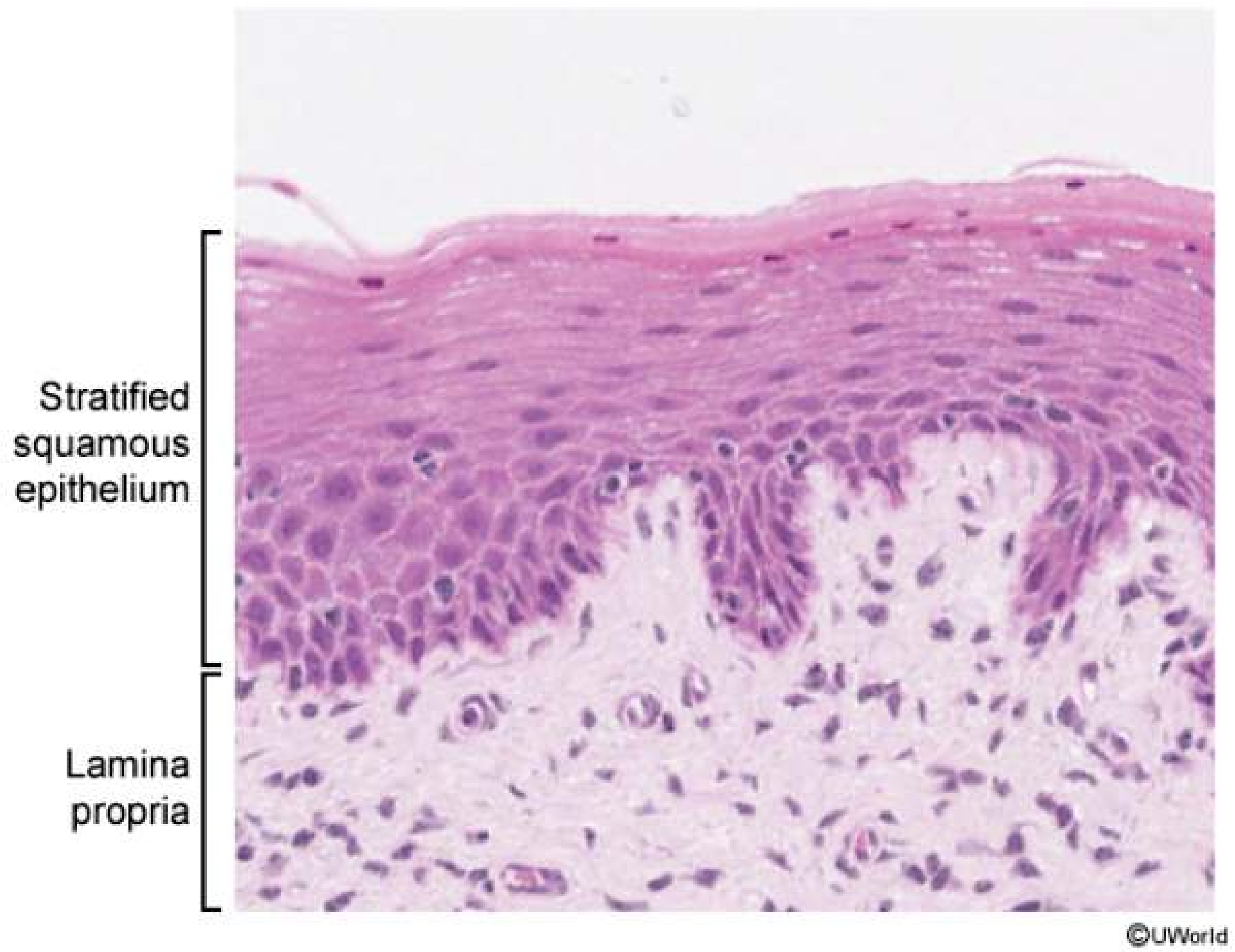
Normal vaginal mucosa



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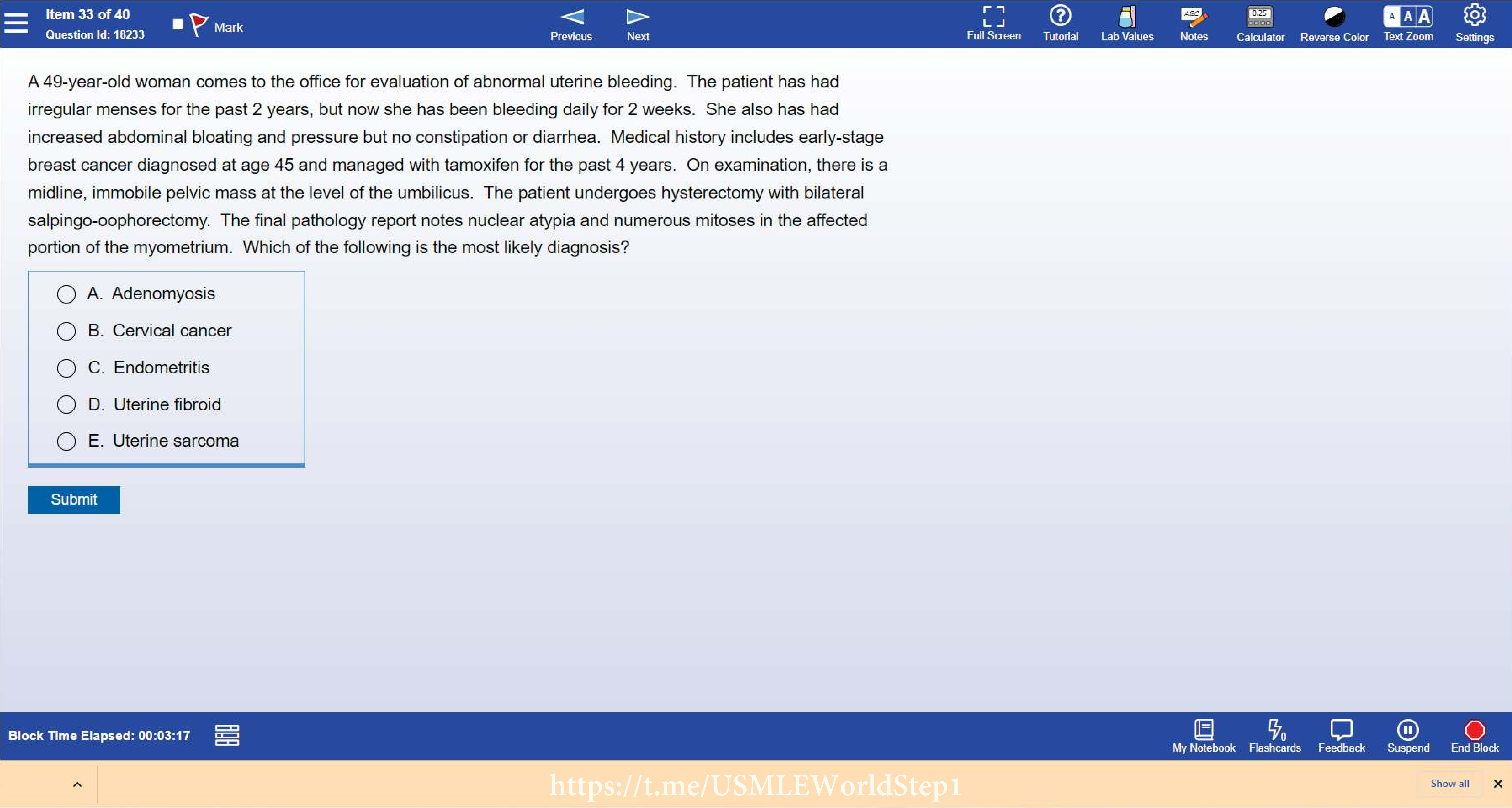
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A 49-year-old woman comes to the office for evaluation of abnormal uterine bleeding. The patient has had irregular menses for the past 2 years, but now she has been bleeding daily for 2 weeks. She also has had increased abdominal bloating and pressure but no constipation or diarrhea. Medical history includes early-stage breast cancer diagnosed at age 45 and managed with tamoxifen for the past 4 years. On examination, there is a midline, immobile pelvic mass at the level of the umbilicus. The patient undergoes hysterectomy with bilateral salpingo-oophorectomy. The final pathology report notes nuclear atypia and numerous mitoses in the affected portion of the myometrium. Which of the following is the most likely diagnosis?

- ○ A. Adenomyosis
- ○ B. Cervical cancer
- ○ C. Endometritis
- ○ D. Uterine fibroid
- ○ E. Uterine sarcoma

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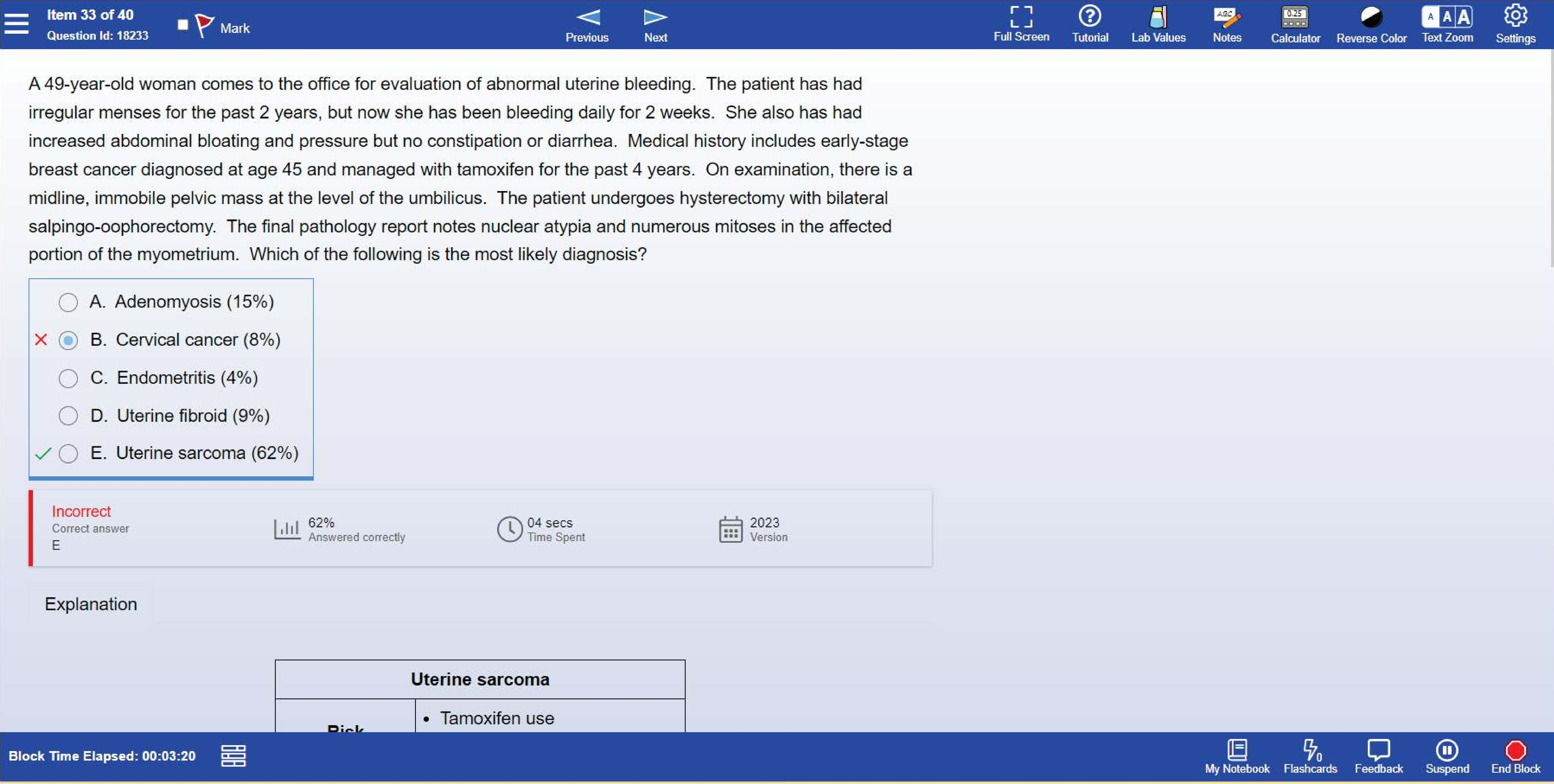
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○ A. Adenomyosis (15%)

✗ ● B. Cervical cancer (8%)

○ C. Endometritis (4%)

○ D. Uterine fibroid (9%)

✓ ○ E. Uterine sarcoma (62%)

Incorrect
Correct answer
E

62%
Answered correctly

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Explanation

Uterine sarcoma	
Risk	• Tamoxifen use

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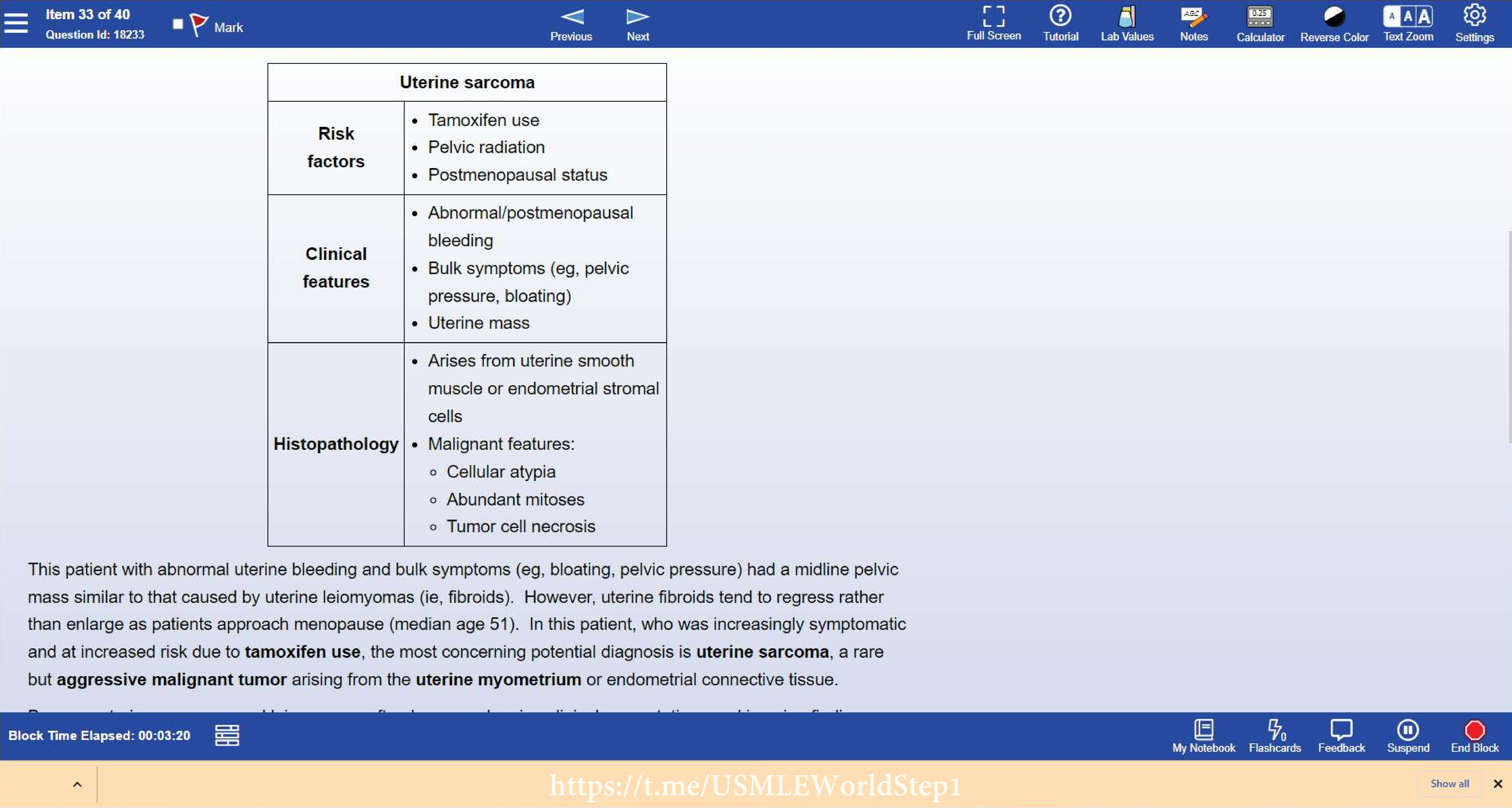
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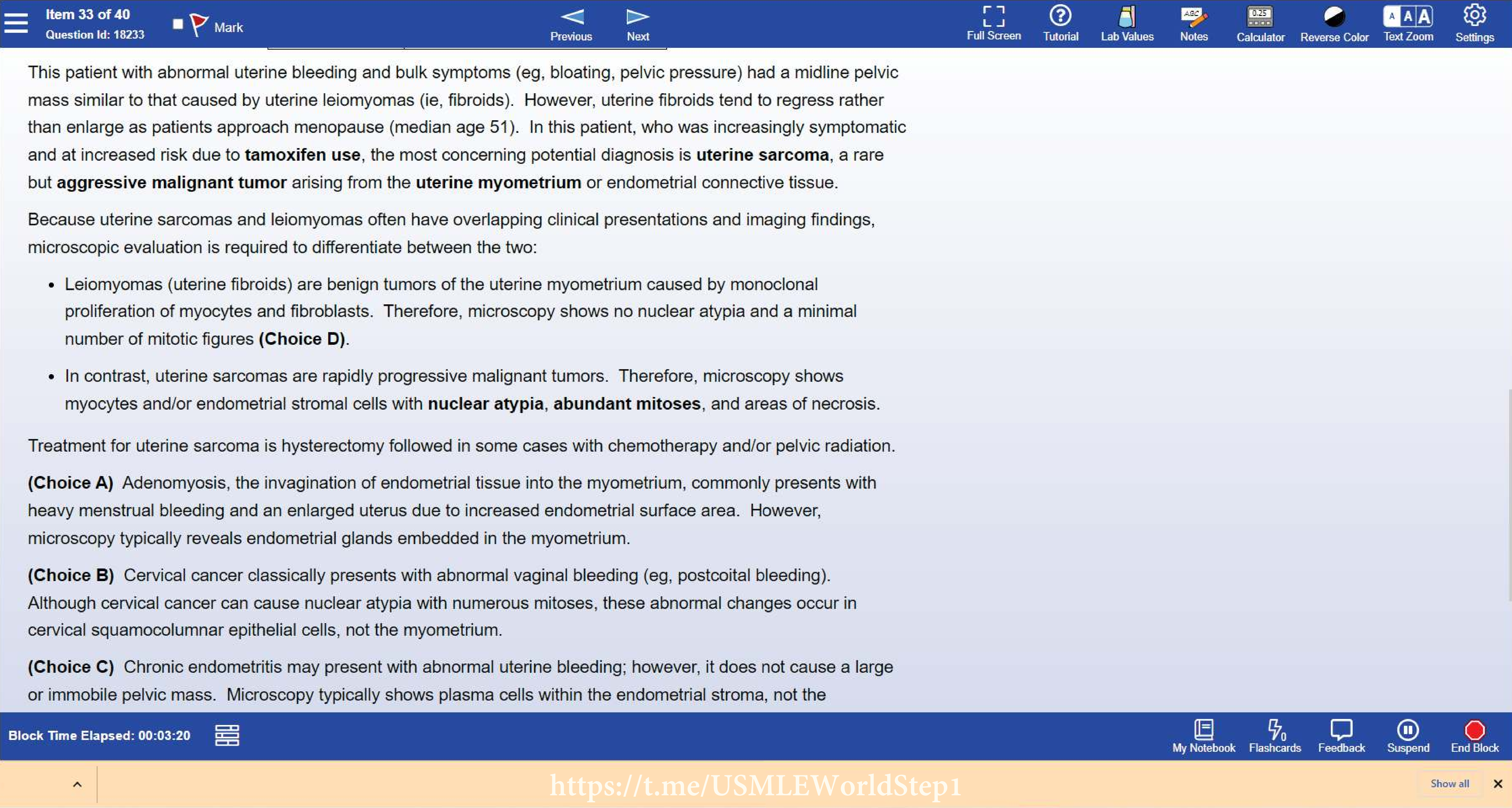
Uterine sarcoma	
Risk factors	• Tamoxifen use • Pelvic radiation • Postmenopausal status
Clinical features	• Abnormal/postmenopausal bleeding • Bulk symptoms (eg, pelvic pressure, bloating) • Uterine mass
Histopathology	• Arises from uterine smooth muscle or endometrial stromal cells • Malignant features: ◦ Cellular atypia ◦ Abundant mitoses ◦ Tumor cell necrosis

This patient with abnormal uterine bleeding and bulk symptoms (eg, bloating, pelvic pressure) had a midline pelvic mass similar to that caused by uterine leiomyomas (ie, fibroids). However, uterine fibroids tend to regress rather than enlarge as patients approach menopause (median age 51). In this patient, who was increasingly symptomatic and at increased risk due to **tamoxifen use**, the most concerning potential diagnosis is **uterine sarcoma**, a rare but **aggressive malignant tumor** arising from the **uterine myometrium** or endometrial connective tissue.



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Because uterine sarcomas and leiomyomas often have overlapping clinical presentations and imaging findings, microscopic evaluation is required to differentiate between the two:

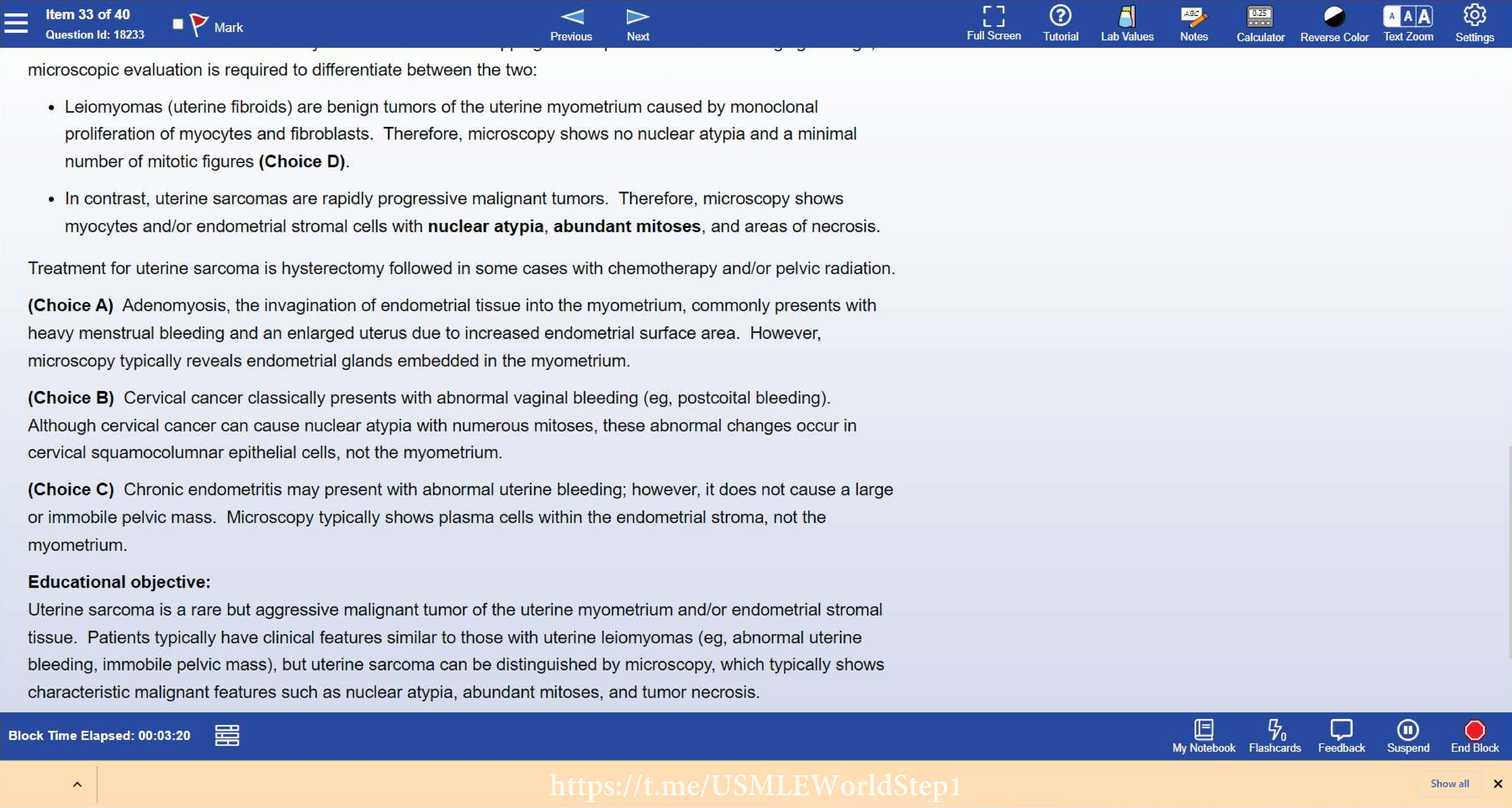
- Leiomyomas (uterine fibroids) are benign tumors of the uterine myometrium caused by monoclonal proliferation of myocytes and fibroblasts. Therefore, microscopy shows no nuclear atypia and a minimal number of mitotic figures **(Choice D)**.
- In contrast, uterine sarcomas are rapidly progressive malignant tumors. Therefore, microscopy shows myocytes and/or endometrial stromal cells with **nuclear atypia**, **abundant mitoses**, and areas of necrosis.

Treatment for uterine sarcoma is hysterectomy followed in some cases with chemotherapy and/or pelvic radiation.

(Choice A) Adenomyosis, the invagination of endometrial tissue into the myometrium, commonly presents with heavy menstrual bleeding and an enlarged uterus due to increased endometrial surface area. However, microscopy typically reveals endometrial glands embedded in the myometrium.

(Choice B) Cervical cancer classically presents with abnormal vaginal bleeding (eg, postcoital bleeding). Although cervical cancer can cause nuclear atypia with numerous mitoses, these abnormal changes occur in cervical squamocolumnar epithelial cells, not the myometrium.

(Choice C) Chronic endometritis may present with abnormal uterine bleeding; however, it does not cause a large or immobile pelvic mass. Microscopy typically shows plasma cells within the endometrial stroma, not the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Educational objective:
Uterine sarcoma is a rare but aggressive malignant tumor of the uterine myometrium and/or endometrial stromal tissue. Patients typically have clinical features similar to those with uterine leiomyomas (eg, abnormal uterine bleeding, immobile pelvic mass), but uterine sarcoma can be distinguished by microscopy, which typically shows characteristic malignant features such as nuclear atypia, abundant mitoses, and tumor necrosis.

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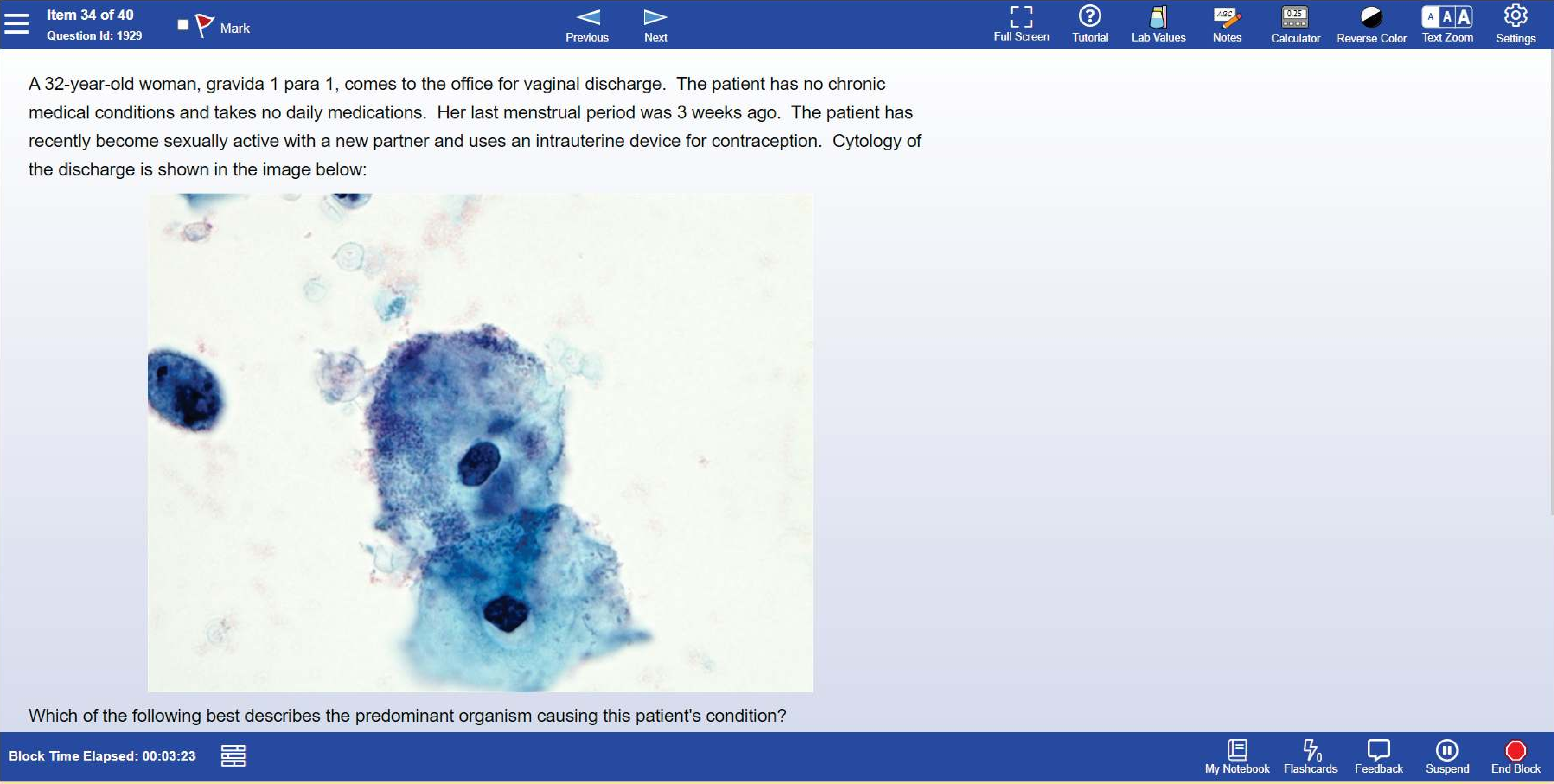
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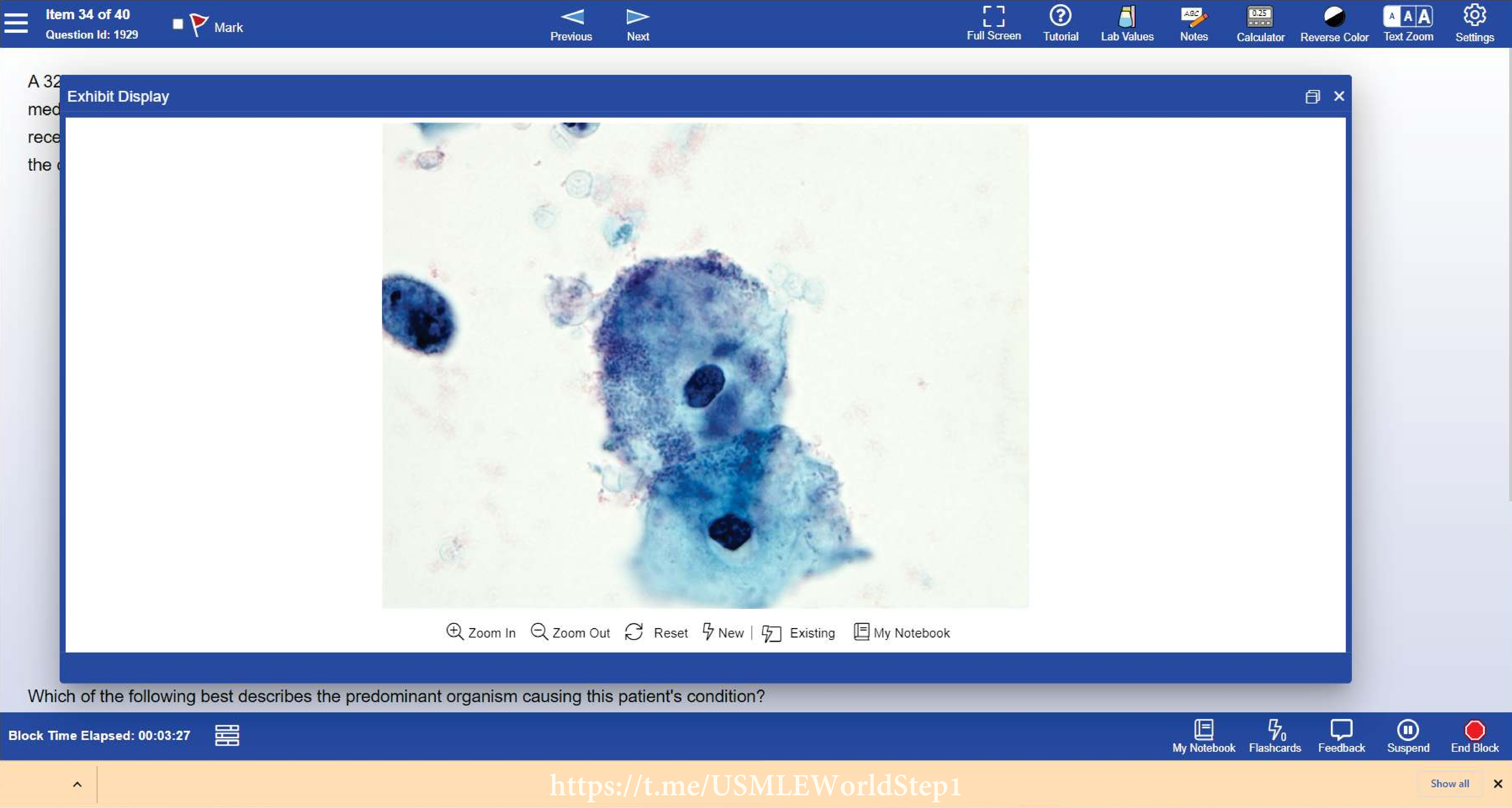
A 32-year-old woman, gravida 1 para 1, comes to the office for vaginal discharge. The patient has no chronic medical conditions and takes no daily medications. Her last menstrual period was 3 weeks ago. The patient has recently become sexually active with a new partner and uses an intrauterine device for contraception. Cytology of the discharge is shown in the image below:

Which of the following best describes the predominant organism causing this patient's condition?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Which of the following best describes the predominant organism causing this patient's condition?

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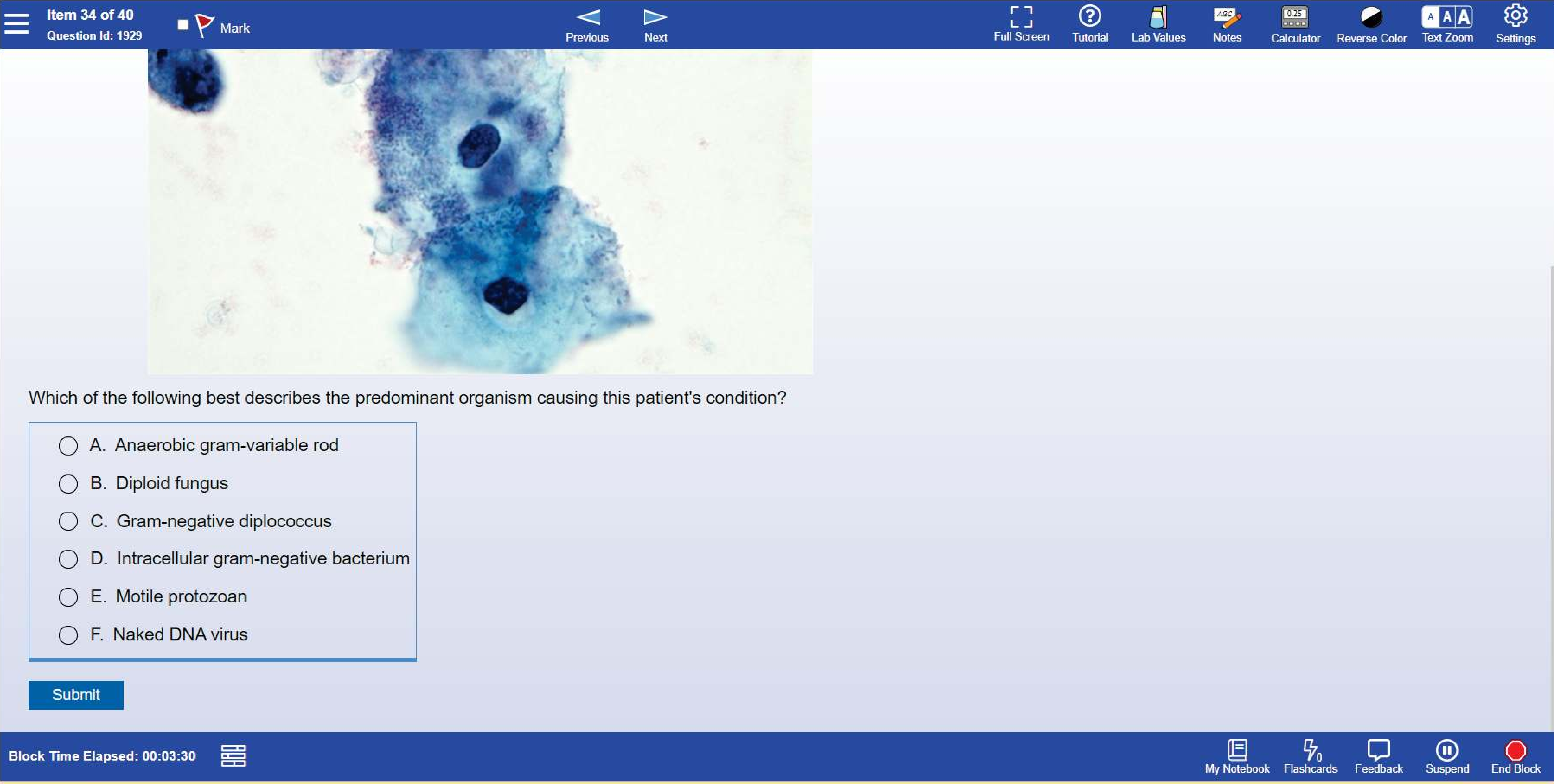
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Which of the following best describes the predominant organism causing this patient's condition?

- ○ A. Anaerobic gram-variable rod
- ○ B. Diploid fungus
- ○ C. Gram-negative diplococcus
- ○ D. Intracellular gram-negative bacterium
- ○ E. Motile protozoan
- ○ F. Naked DNA virus

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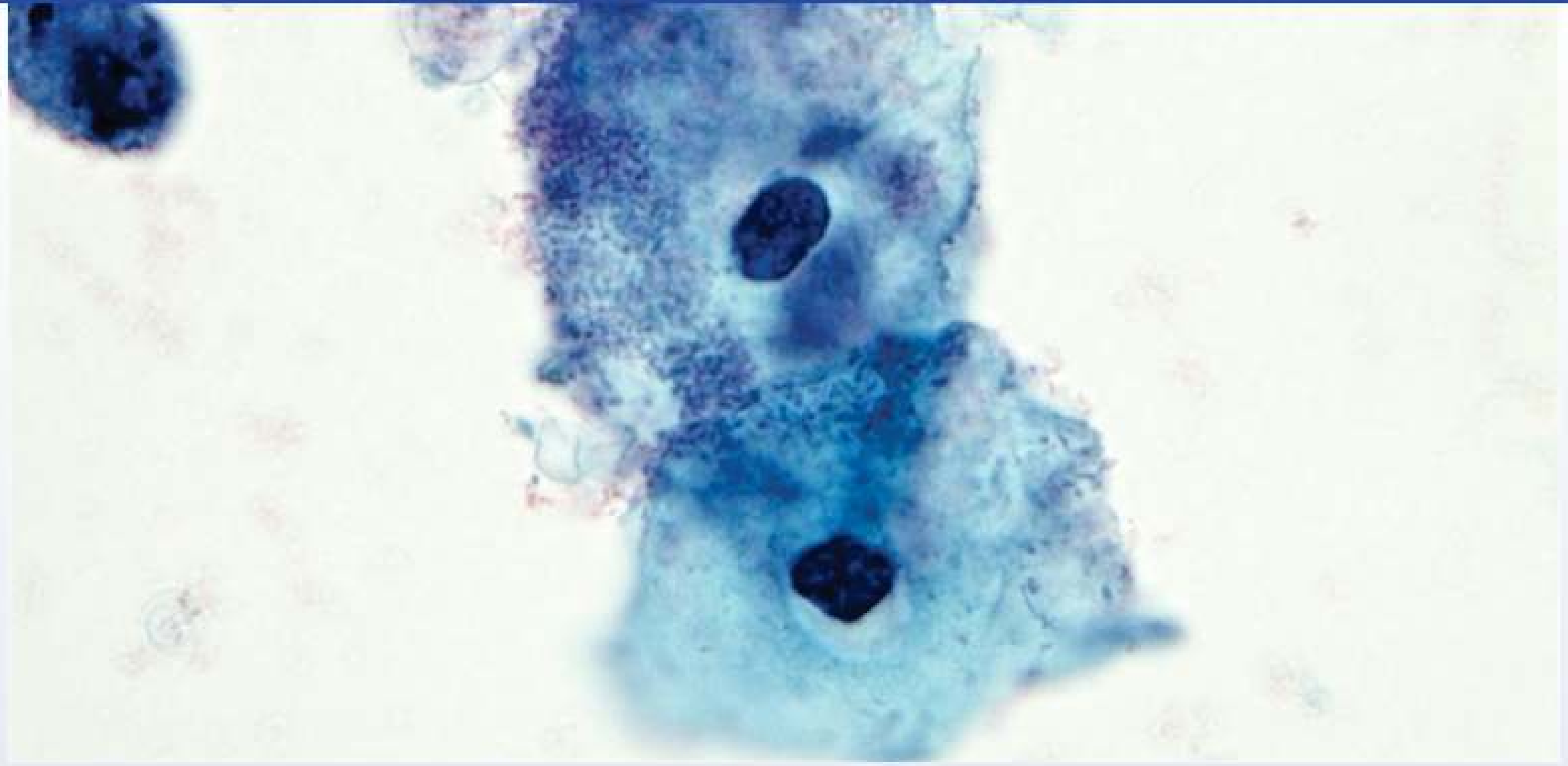

Which of the following best describes the predominant organism causing this patient's condition?

- ✓ ○ A. Anaerobic gram-variable rod (56%)
- ○ B. Diploid fungus (2%)
- ✗ ● C. Gram-negative diplococcus (6%)
- ○ D. Intracellular gram-negative bacterium (13%)
- ○ E. Motile protozoan (9%)
- ○ F. Naked DNA virus (11%)

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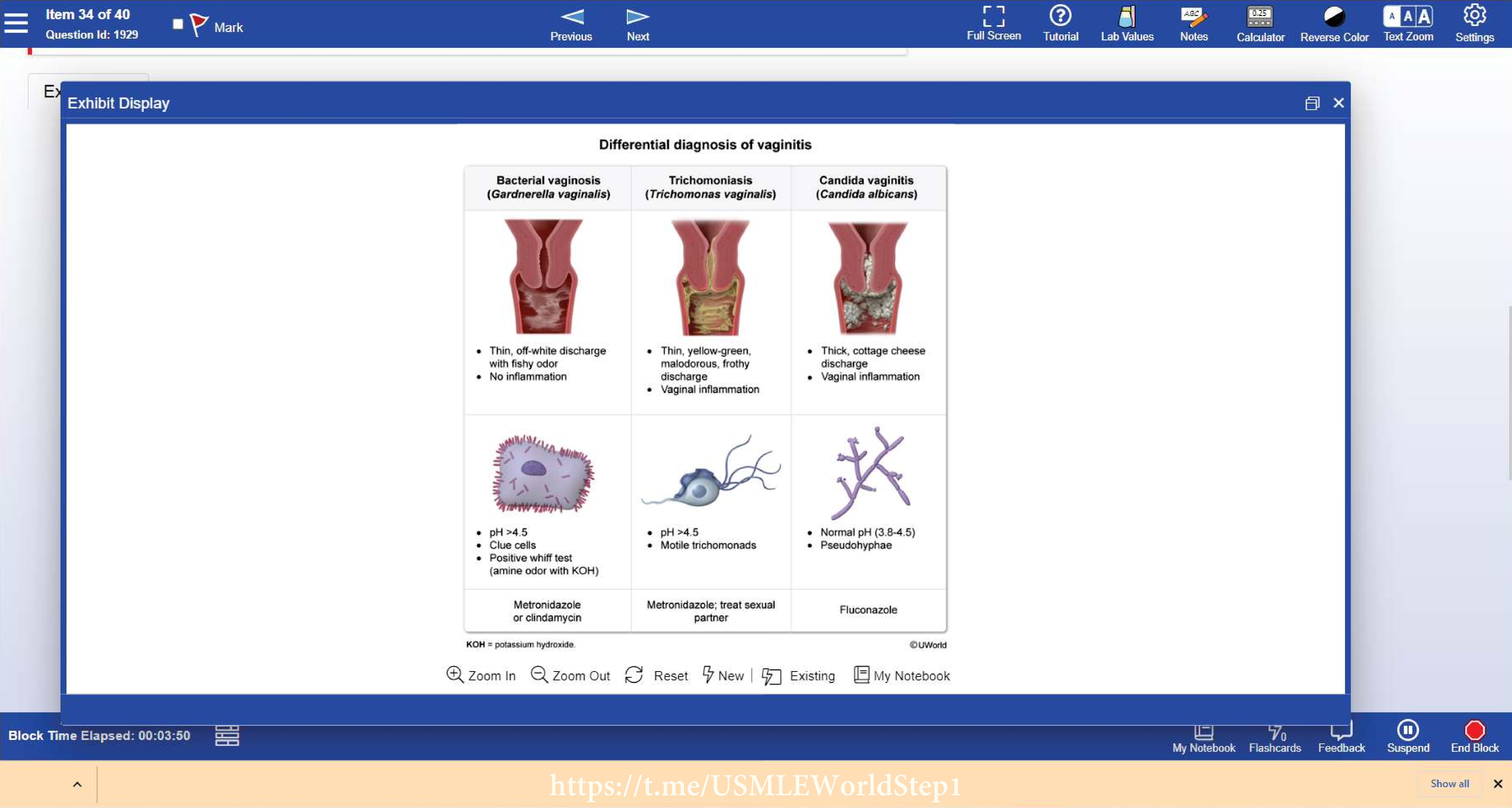
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Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	Trichomoniasis (*Trichomonas vaginalis*)	Candida vaginitis (*Candida albicans*)
• Thin, off-white discharge with fishy odor • No inflammation	• Thin, yellow-green, malodorous, frothy discharge • Vaginal inflammation	• Thick, cottage cheese discharge • Vaginal inflammation
• pH >4.5 • Clue cells • Positive whiff test (amine odor with KOH)	• pH >4.5 • Motile trichomonads	• Normal pH (3.8-4.5) • Pseudohyphae
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

KOH = potassium hydroxide.

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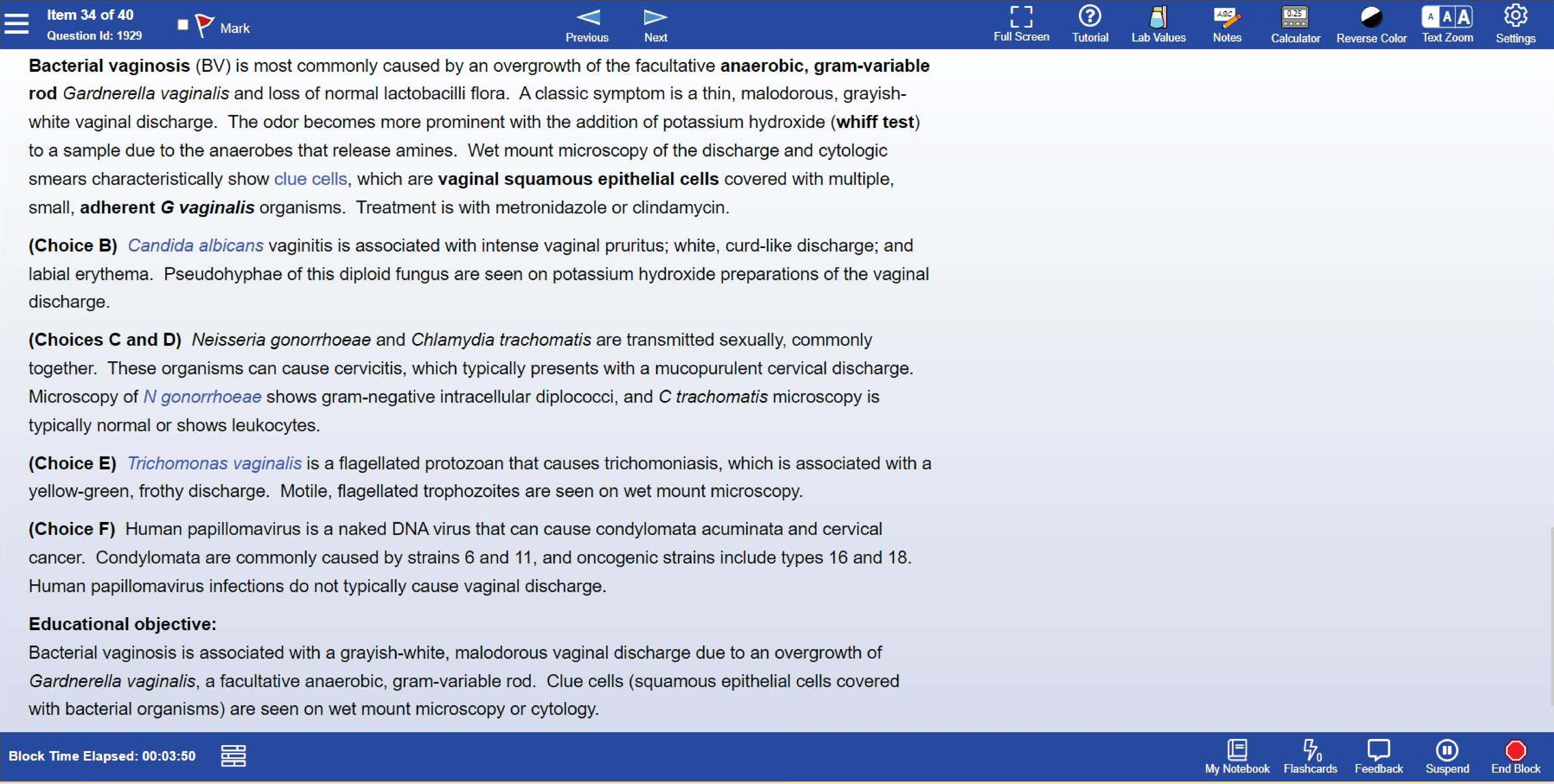

Bacterial vaginosis (BV) is most commonly caused by an overgrowth of the facultative **anaerobic, gram-variable rod** *Gardnerella vaginalis* and loss of normal lactobacilli flora. A classic symptom is a thin, malodorous, grayish-white vaginal discharge. The odor becomes more prominent with the addition of potassium hydroxide (**whiff test**) to a sample due to the anaerobes that release amines. Wet mount microscopy of the discharge and cytologic smears characteristically show clue cells, which are **vaginal squamous epithelial cells** covered with multiple, small, **adherent *G vaginalis*** organisms. Treatment is with metronidazole or clindamycin.

(Choice B) *Candida albicans* vaginitis is associated with intense vaginal pruritus; white, curd-like discharge; and labial erythema. Pseudohyphae of this diploid fungus are seen on potassium hydroxide preparations of the vaginal discharge.

(Choices C and D) *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are transmitted sexually, commonly together. These organisms can cause cervicitis, which typically presents with a mucopurulent cervical discharge. Microscopy of *N gonorrhoeae* shows gram-negative intracellular diplococci, and *C trachomatis* microscopy is typically normal or shows leukocytes.

(Choice E) *Trichomonas vaginalis* is a flagellated protozoan that causes trichomoniasis, which is associated with a yellow-green, frothy discharge. Motile, flagellated trophozoites are seen on wet mount microscopy.

(Choice F) Human papillomavirus is a naked DNA virus that can cause condylomata acuminata and cervical cancer. Condylomata are commonly caused by strains 6 and 11, and oncogenic strains include types 16 and 18. Human papillomavirus infections do not typically cause vaginal discharge.

Educational objective:

Bacterial vaginosis is associated with a grayish-white, malodorous vaginal discharge due to an overgrowth of *Gardnerella vaginalis*, a facultative anaerobic, gram-variable rod. Clue cells (squamous epithelial cells covered with bacterial organisms) are seen on wet mount microscopy or cytology.

Bacterial vaginosis (BV) is most commonly caused by an overgrowth of the facultative **anaerobic, gram-variable rod**

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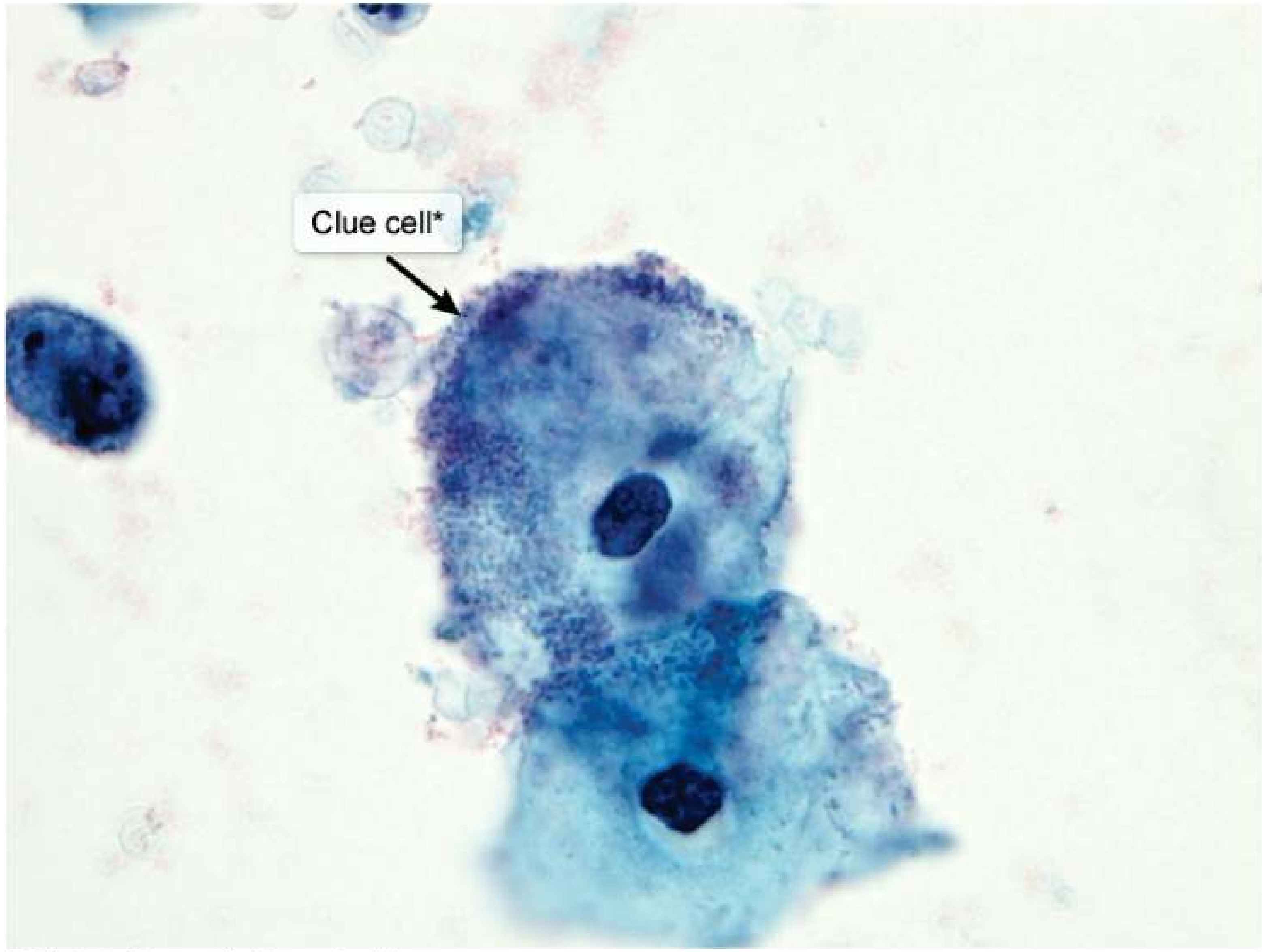
Bacterial vaginosis



*Epithelial cell covered with coccobacilli.

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Bacterial vaginosis (BV) is most commonly caused by an overgrowth of the facultative **anaerobic, gram-variable rod**

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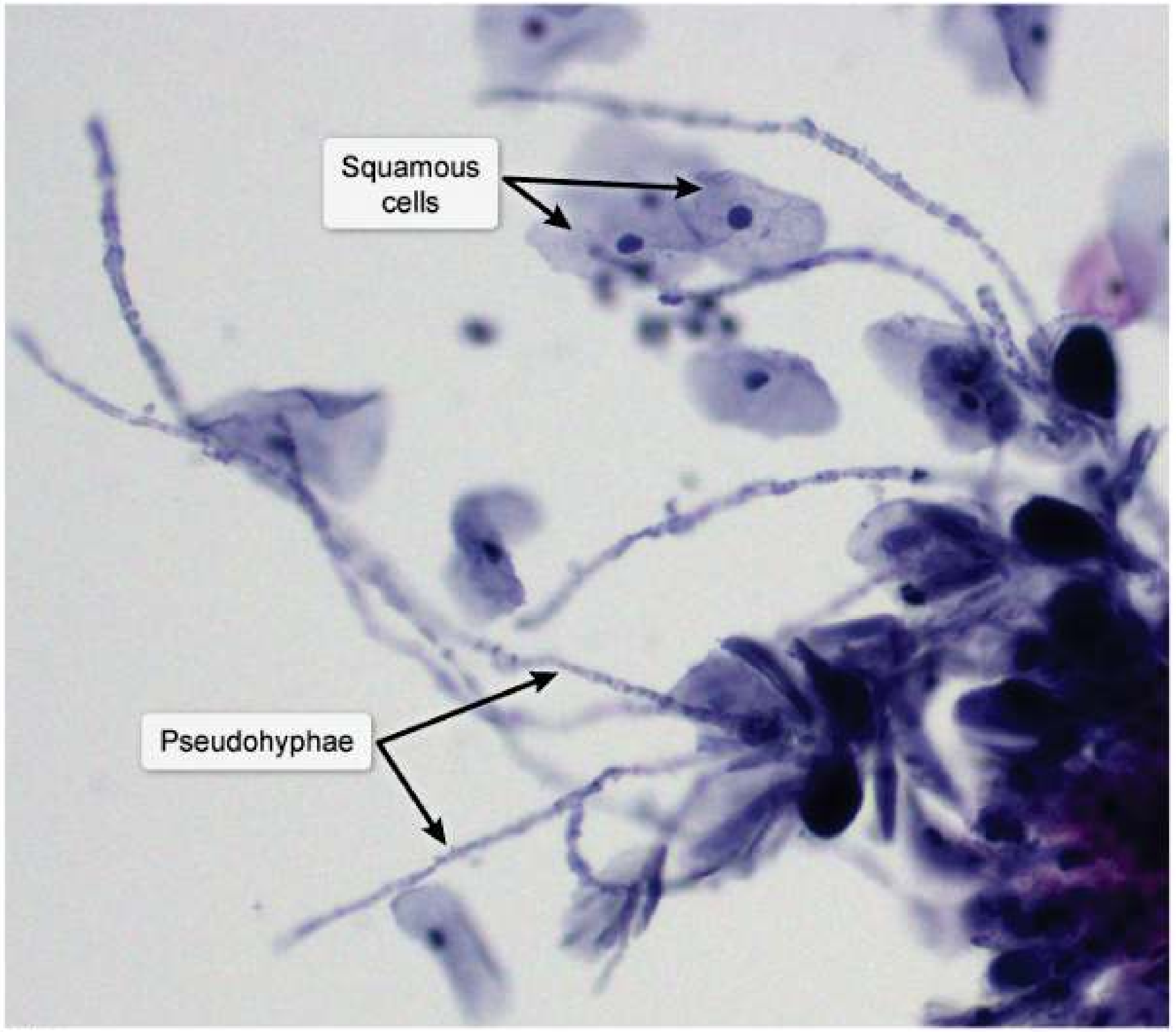
Exhibit Display

Candida


Squamous cells
Pseudohyphae

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Bacterial vaginosis (BV) is most commonly caused by an overgrowth of the facultative **anaerobic, gram-variable rod**

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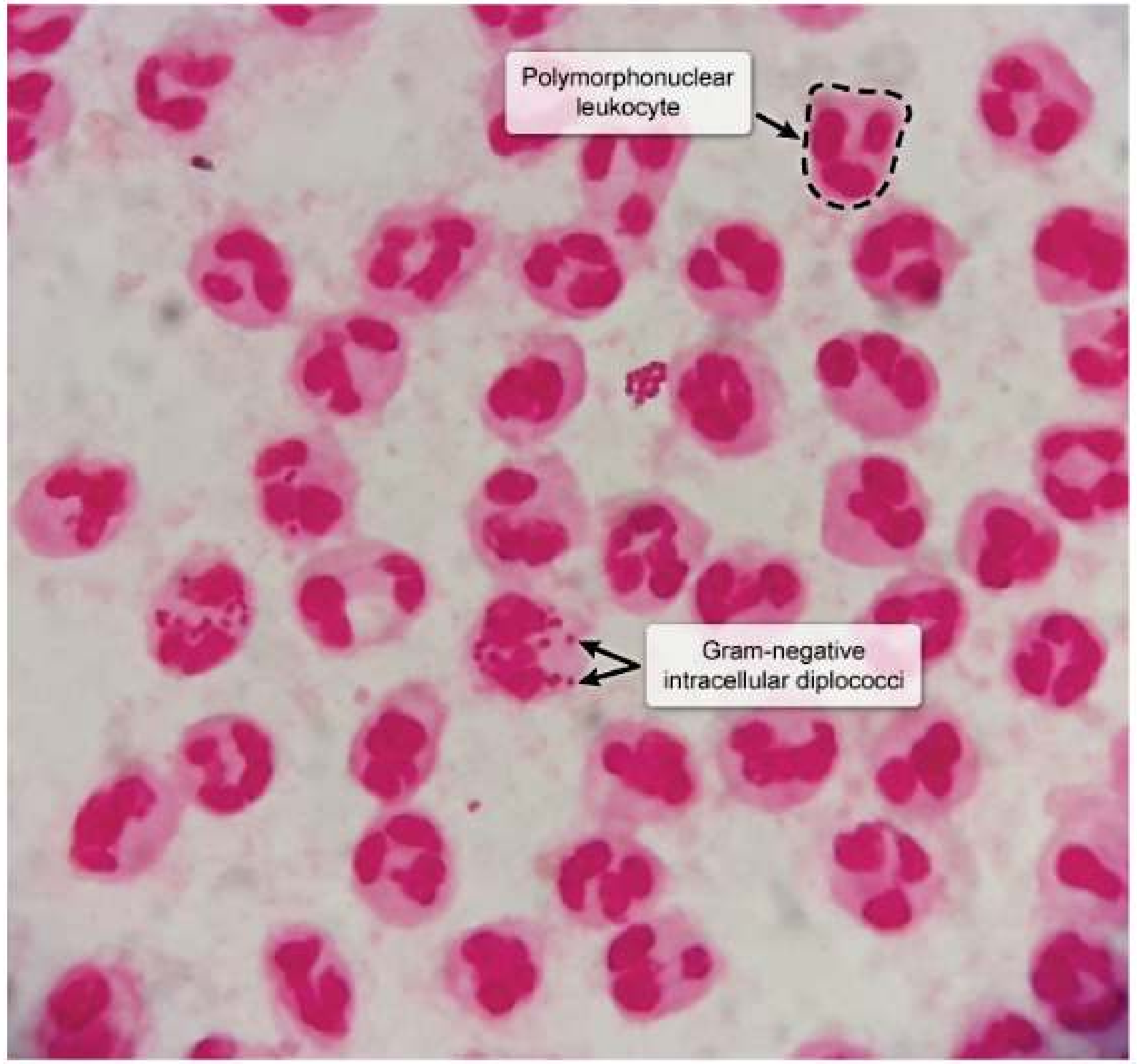
Neisseria gonorrhoeae


Polymorphonuclear leukocyte
Gram-negative intracellular diplococci

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Bacterial vaginosis (BV) is most commonly caused by an overgrowth of the facultative **anaerobic, gram-variable**

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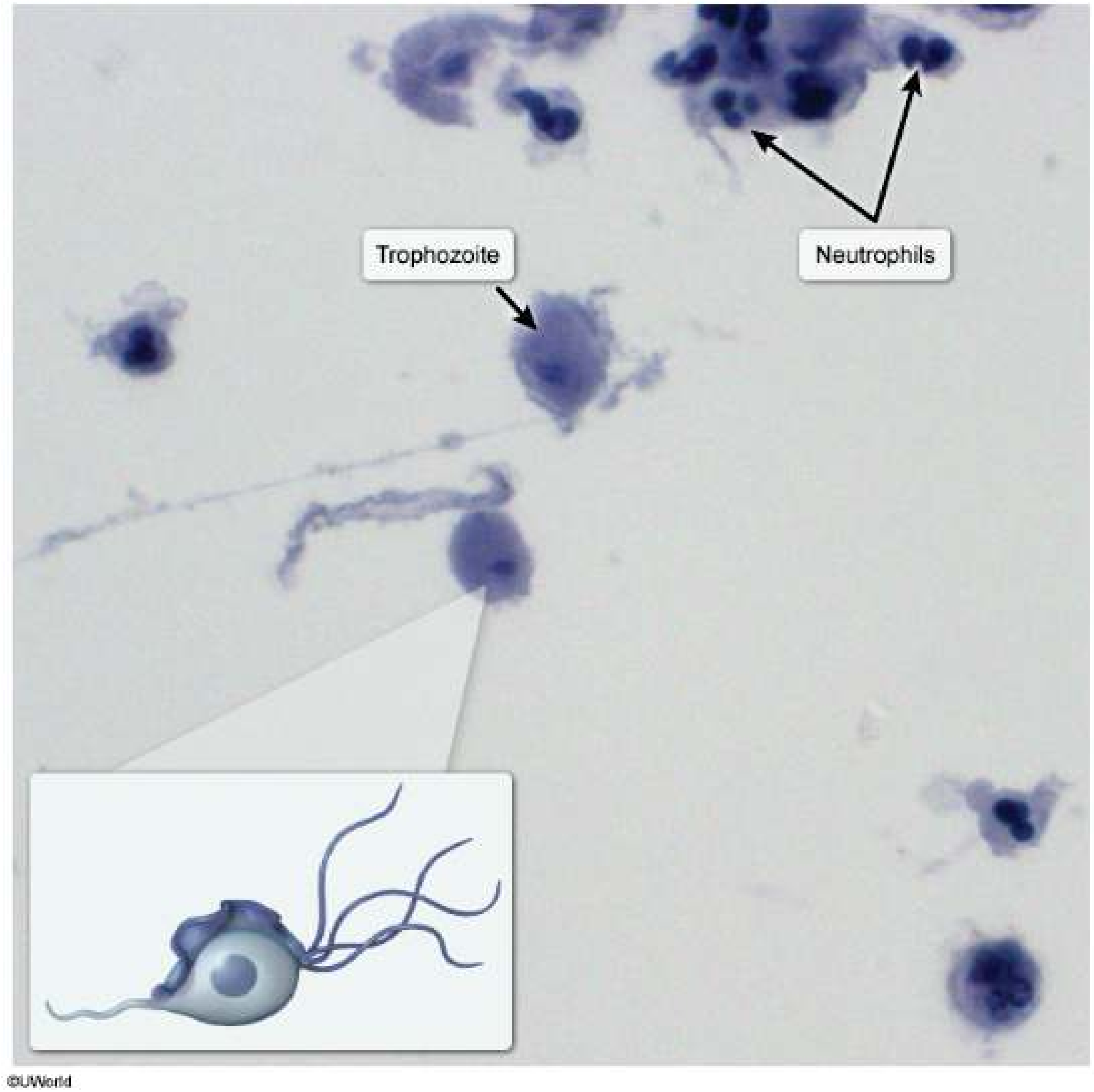
Trichomonas vaginalis



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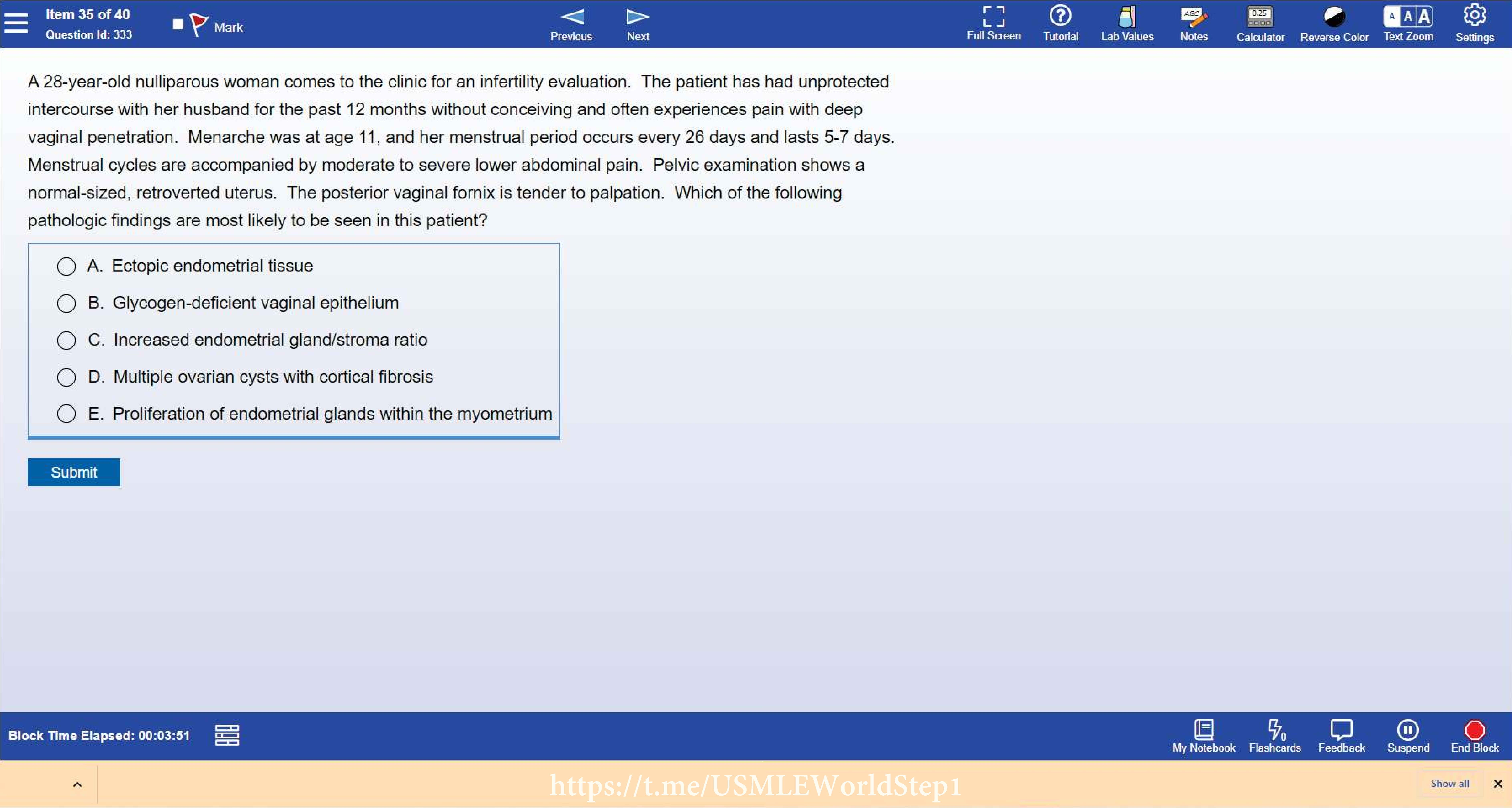
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A 28-year-old nulliparous woman comes to the clinic for an infertility evaluation. The patient has had unprotected intercourse with her husband for the past 12 months without conceiving and often experiences pain with deep vaginal penetration. Menarche was at age 11, and her menstrual period occurs every 26 days and lasts 5-7 days. Menstrual cycles are accompanied by moderate to severe lower abdominal pain. Pelvic examination shows a normal-sized, retroverted uterus. The posterior vaginal fornix is tender to palpation. Which of the following pathologic findings are most likely to be seen in this patient?

- ○ A. Ectopic endometrial tissue
- ○ B. Glycogen-deficient vaginal epithelium
- ○ C. Increased endometrial gland/stroma ratio
- ○ D. Multiple ovarian cysts with cortical fibrosis
- ○ E. Proliferation of endometrial glands within the myometrium

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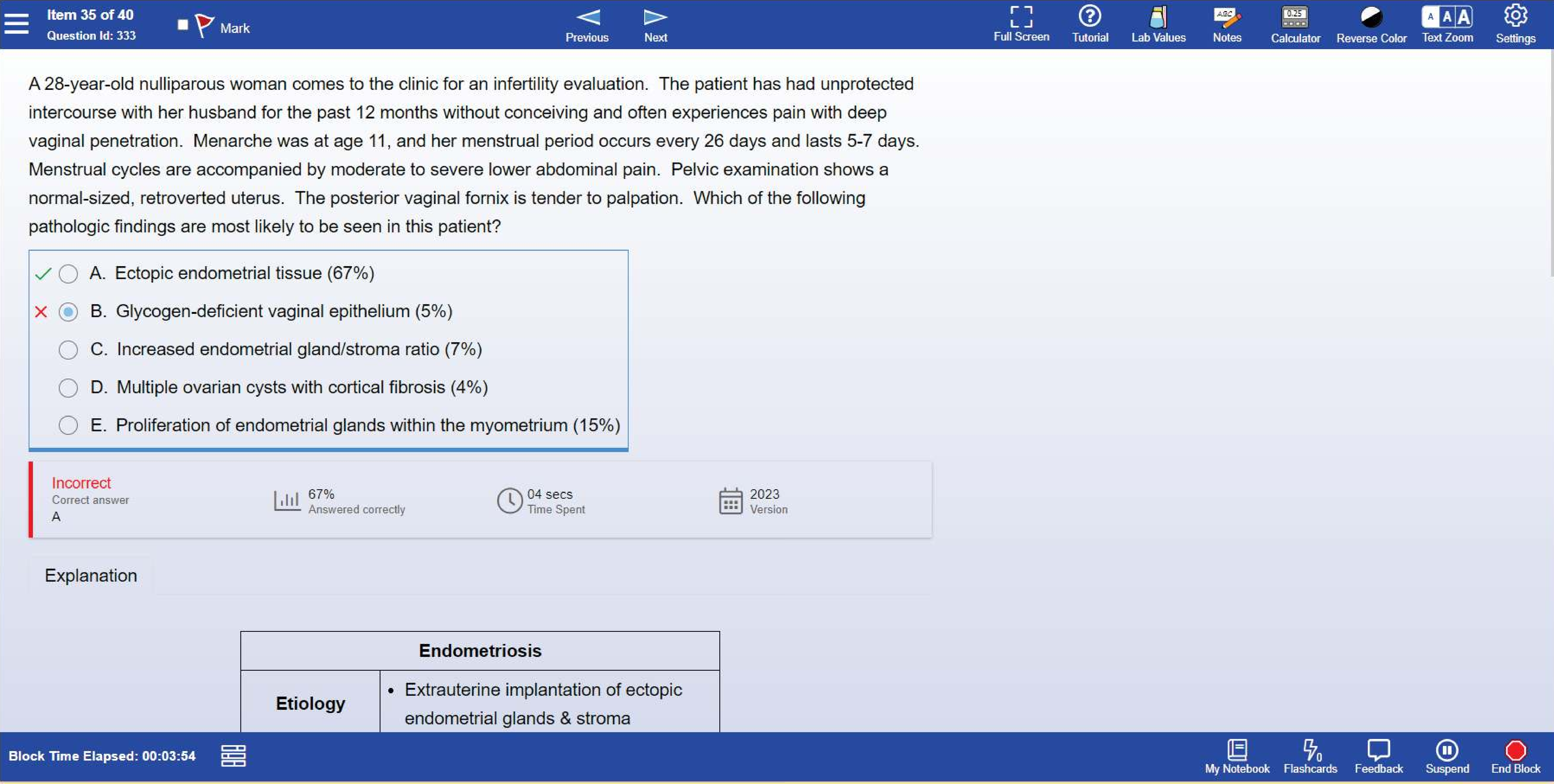
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✓ ○ A. Ectopic endometrial tissue (67%)

✗ ● B. Glycogen-deficient vaginal epithelium (5%)

○ C. Increased endometrial gland/stroma ratio (7%)

○ D. Multiple ovarian cysts with cortical fibrosis (4%)

○ E. Proliferation of endometrial glands within the myometrium (15%)

Incorrect
Correct answer
A

67%
Answered correctly

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Explanation

Endometriosis	
Etiology	• Extrauterine implantation of ectopic endometrial glands & stroma

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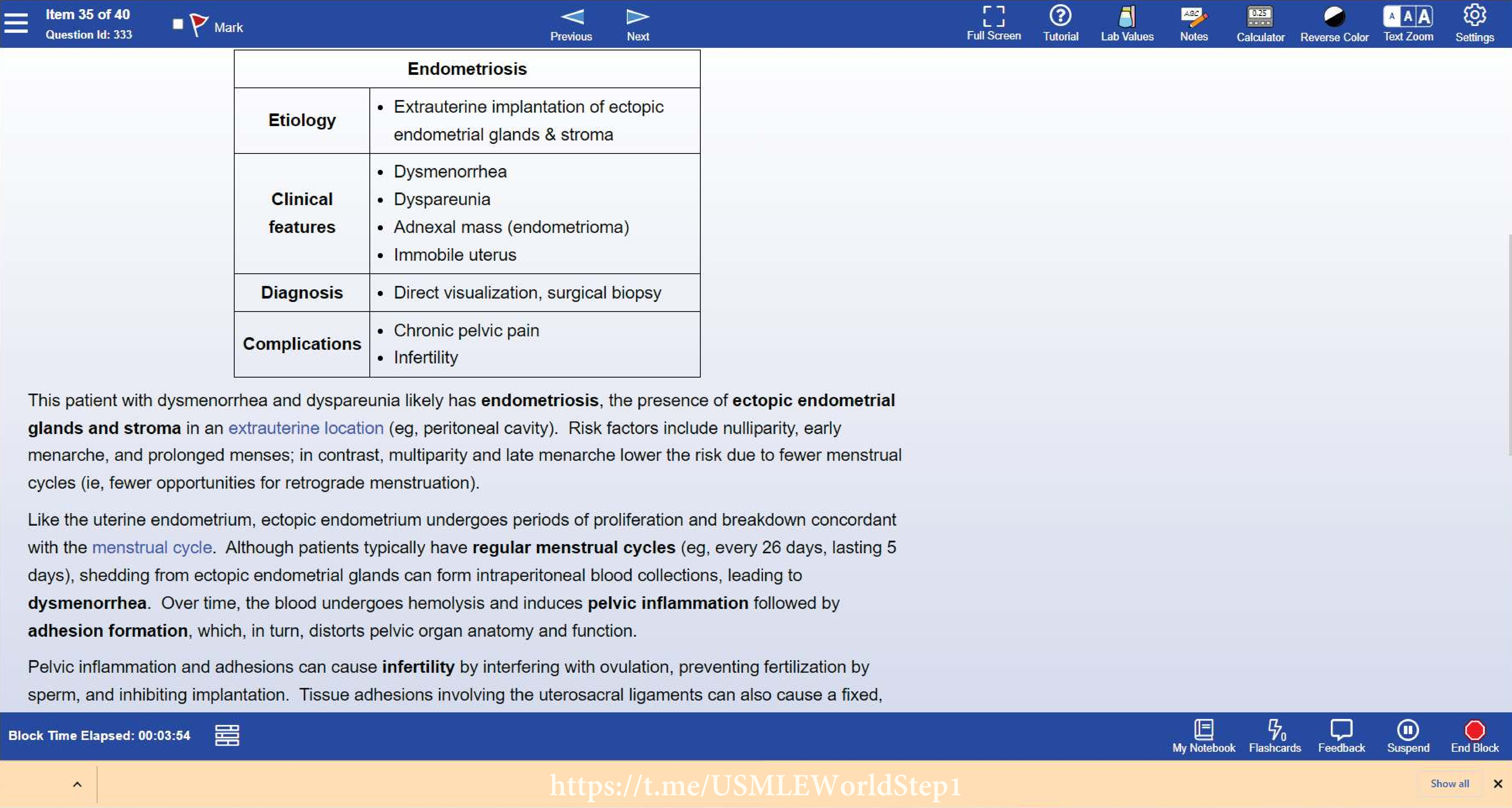
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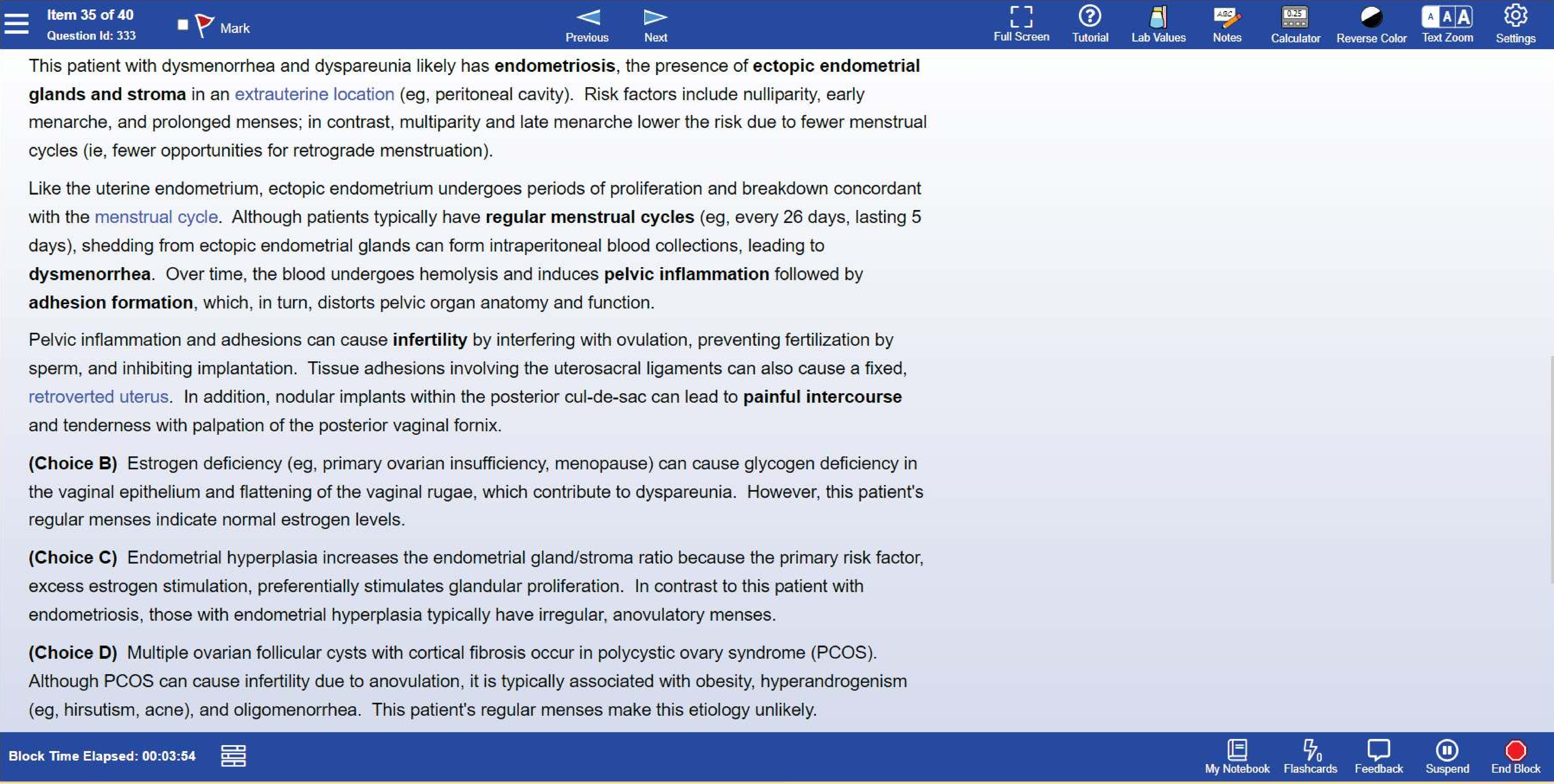
Endometriosis	
Etiology	• Extrauterine implantation of ectopic endometrial glands & stroma
Clinical features	• Dysmenorrhea • Dyspareunia • Adnexal mass (endometrioma) • Immobile uterus
Diagnosis	• Direct visualization, surgical biopsy
Complications	• Chronic pelvic pain • Infertility

This patient with dysmenorrhea and dyspareunia likely has **endometriosis**, the presence of **ectopic endometrial glands and stroma** in an extrauterine location (eg, peritoneal cavity). Risk factors include nulliparity, early menarche, and prolonged menses; in contrast, multiparity and late menarche lower the risk due to fewer menstrual cycles (ie, fewer opportunities for retrograde menstruation).

Like the uterine endometrium, ectopic endometrium undergoes periods of proliferation and breakdown concordant with the menstrual cycle. Although patients typically have **regular menstrual cycles** (eg, every 26 days, lasting 5 days), shedding from ectopic endometrial glands can form intraperitoneal blood collections, leading to **dysmenorrhea**. Over time, the blood undergoes hemolysis and induces **pelvic inflammation** followed by **adhesion formation**, which, in turn, distorts pelvic organ anatomy and function.

Pelvic inflammation and adhesions can cause **infertility** by interfering with ovulation, preventing fertilization by sperm, and inhibiting implantation. Tissue adhesions involving the uterosacral ligaments can also cause a fixed,



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Pelvic inflammation and adhesions can cause **infertility** by interfering with ovulation, preventing fertilization by sperm, and inhibiting implantation. Tissue adhesions involving the uterosacral ligaments can also cause a fixed, retroverted uterus. In addition, nodular implants within the posterior cul-de-sac can lead to **painful intercourse** and tenderness with palpation of the posterior vaginal fornix.

(Choice B) Estrogen deficiency (eg, primary ovarian insufficiency, menopause) can cause glycogen deficiency in the vaginal epithelium and flattening of the vaginal rugae, which contribute to dyspareunia. However, this patient's regular menses indicate normal estrogen levels.

(Choice C) Endometrial hyperplasia increases the endometrial gland/stroma ratio because the primary risk factor, excess estrogen stimulation, preferentially stimulates glandular proliferation. In contrast to this patient with endometriosis, those with endometrial hyperplasia typically have irregular, anovulatory menses.

(Choice D) Multiple ovarian follicular cysts with cortical fibrosis occur in polycystic ovary syndrome (PCOS). Although PCOS can cause infertility due to anovulation, it is typically associated with obesity, hyperandrogenism (eg, hirsutism, acne), and oligomenorrhea. This patient's regular menses make this etiology unlikely.

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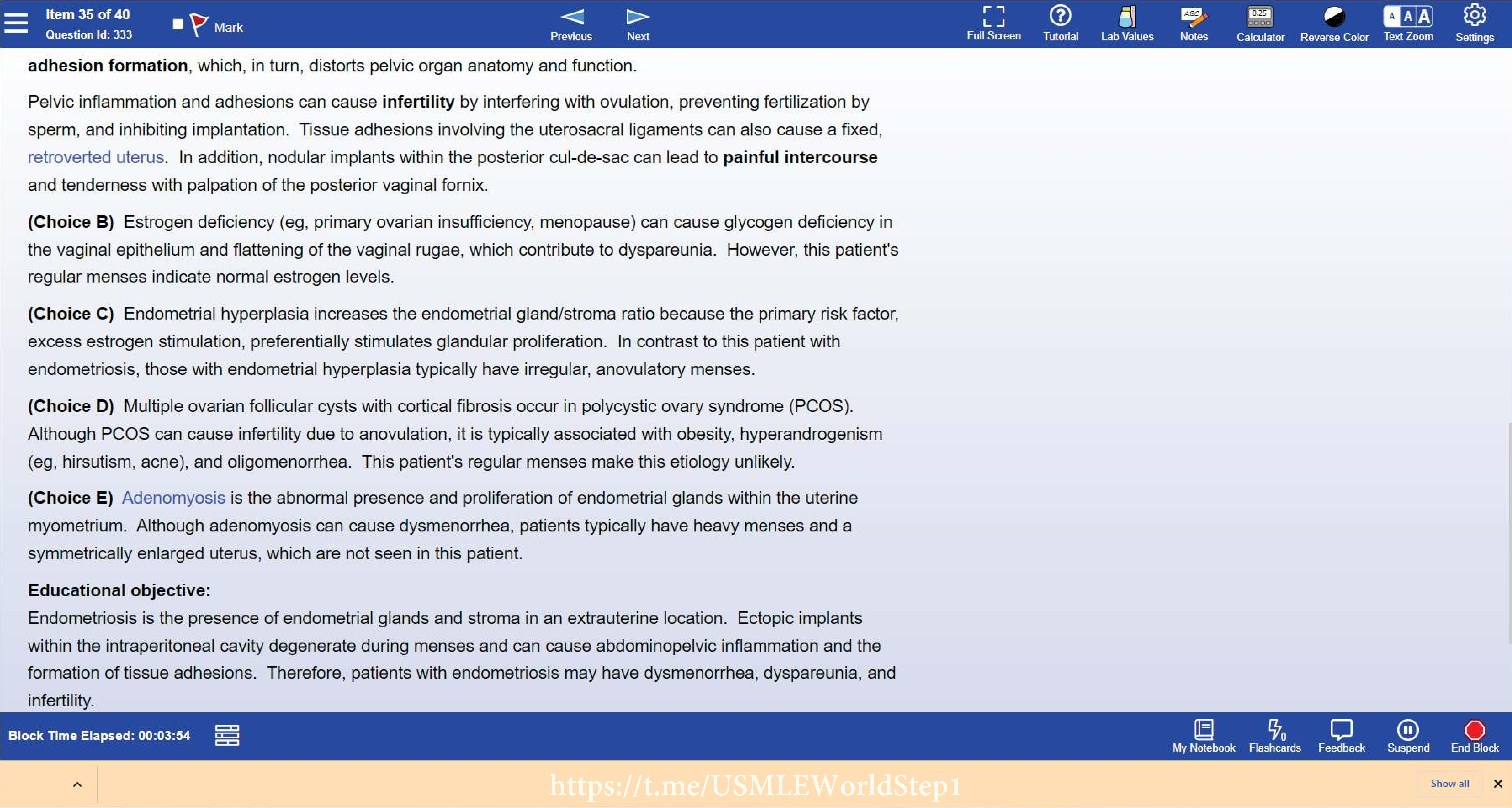

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Question Id: 333

adhesion formation, which, in turn, distorts pelvic organ anatomy and function.

Pelvic inflammation and adhesions can cause **infertility** by interfering with ovulation, preventing fertilization by sperm, and inhibiting implantation. Tissue adhesions involving the uterosacral ligaments can also cause a fixed, retroverted uterus. In addition, nodular implants within the posterior cul-de-sac can lead to **painful intercourse** and tenderness with palpation of the posterior vaginal fornix.

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(Choice E) Adenomyosis is the abnormal presence and proliferation of endometrial glands within the uterine myometrium. Although adenomyosis can cause dysmenorrhea, patients typically have heavy menses and a symmetrically enlarged uterus, which are not seen in this patient.

Educational objective:
Endometriosis is the presence of endometrial glands and stroma in an extrauterine location. Ectopic implants within the intraperitoneal cavity degenerate during menses and can cause abdominopelvic inflammation and the formation of tissue adhesions. Therefore, patients with endometriosis may have dysmenorrhea, dyspareunia, and infertility.

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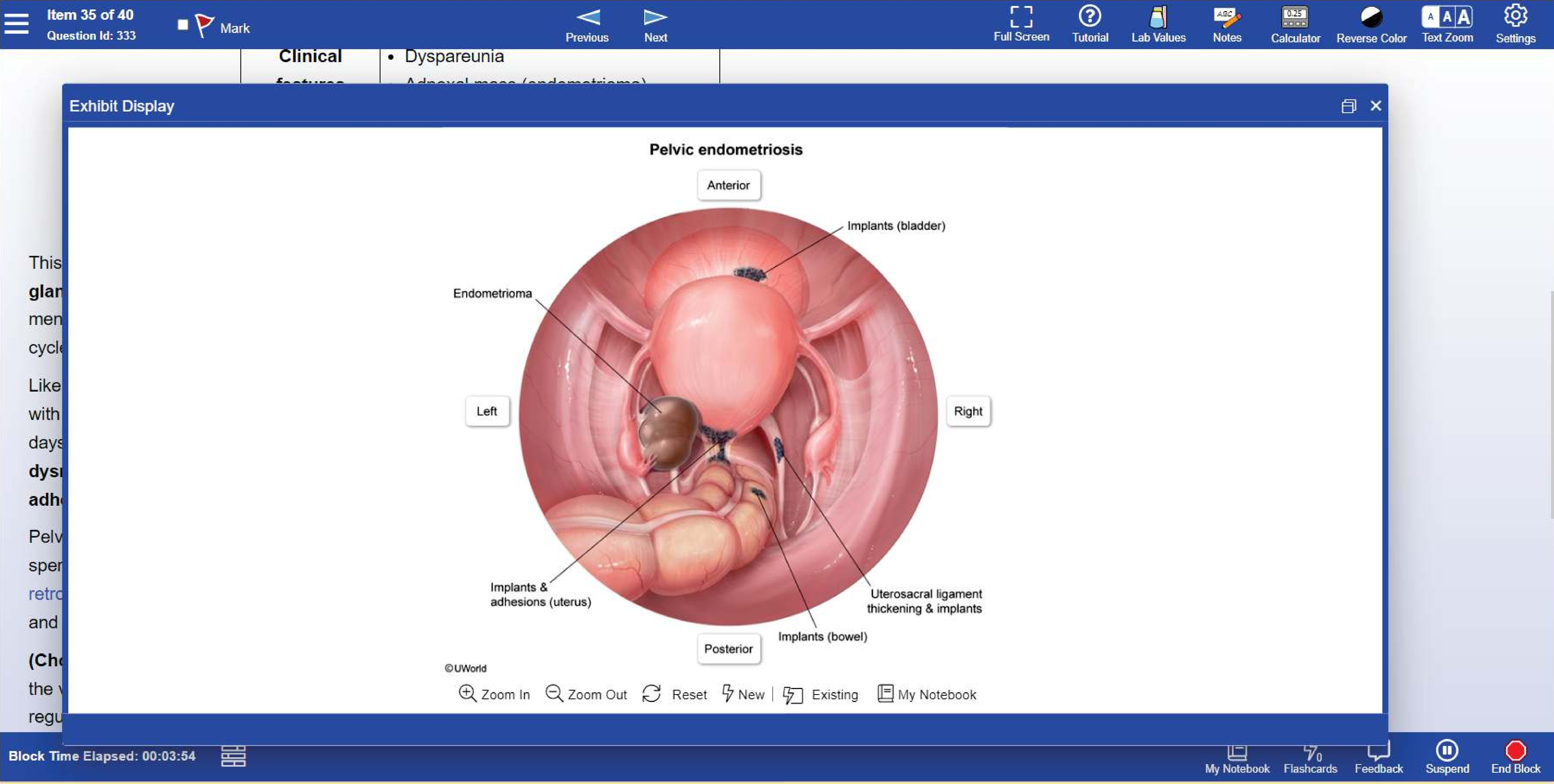

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Exhibit Display
Anterior
Implants (bladder)
Endometrioma
Left
Right
Implants &
adhesions (uterus)
Uterosacral ligament
thickening & implants
Implants (bowel)
Posterior
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Clinical features

- Dyspareunia
- Adnexal mass (endometrioma)

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Pelvic endometriosis

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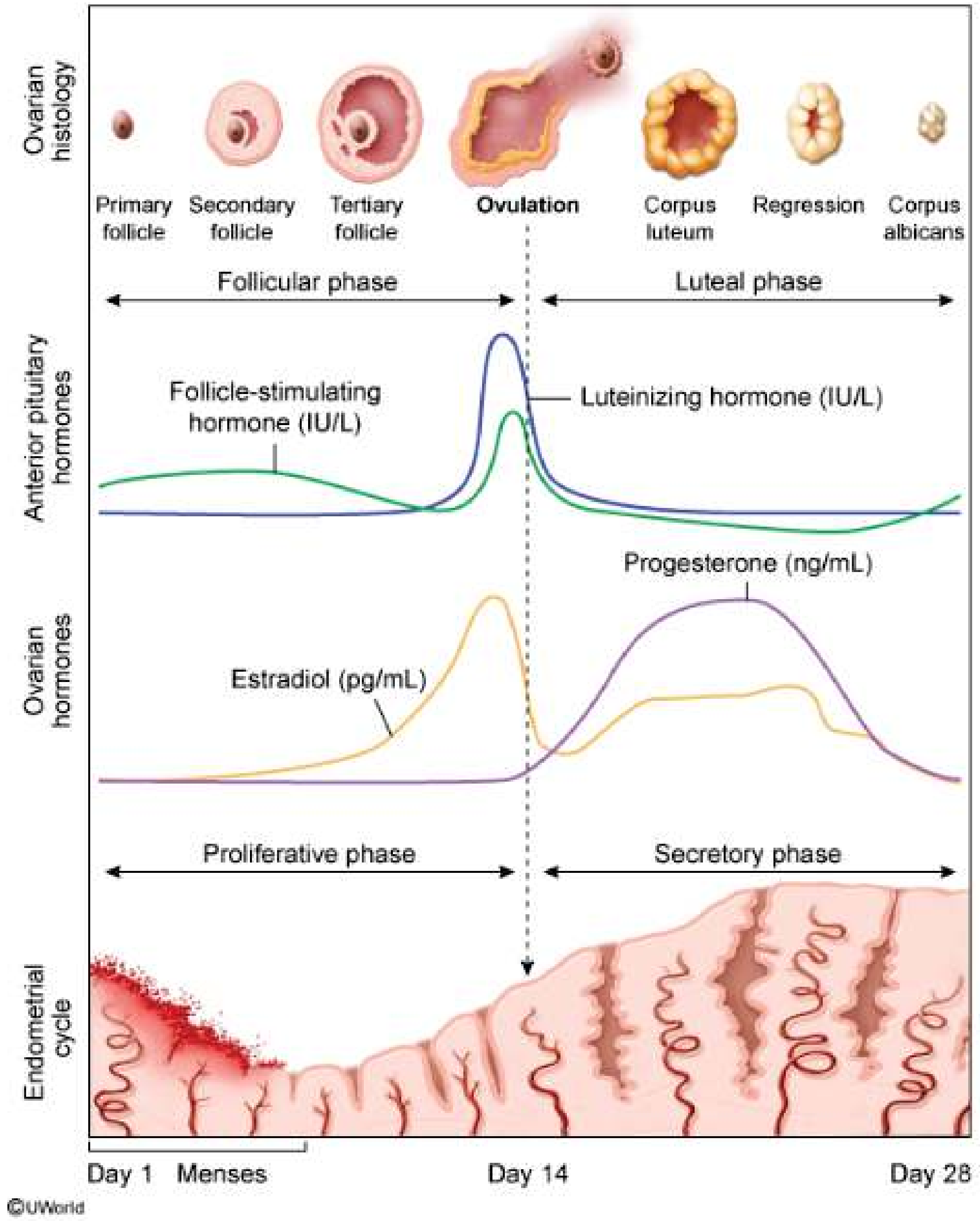
Menstrual cycle


Ovarian histology
Primary follicle
Secondary follicle
Tertiary follicle
Ovulation
Corpus luteum
Regression
Corpus albicans
Follicular phase
Luteal phase
Anterior pituitary hormones
Follicle-stimulating hormone (IU/L)
Luteinizing hormone (IU/L)
Ovarian hormones
Progesterone (ng/mL)
Estradiol (pg/mL)
Proliferative phase
Secretory phase
Endometrial cycle
Day 1
Menses
Day 14
Day 28
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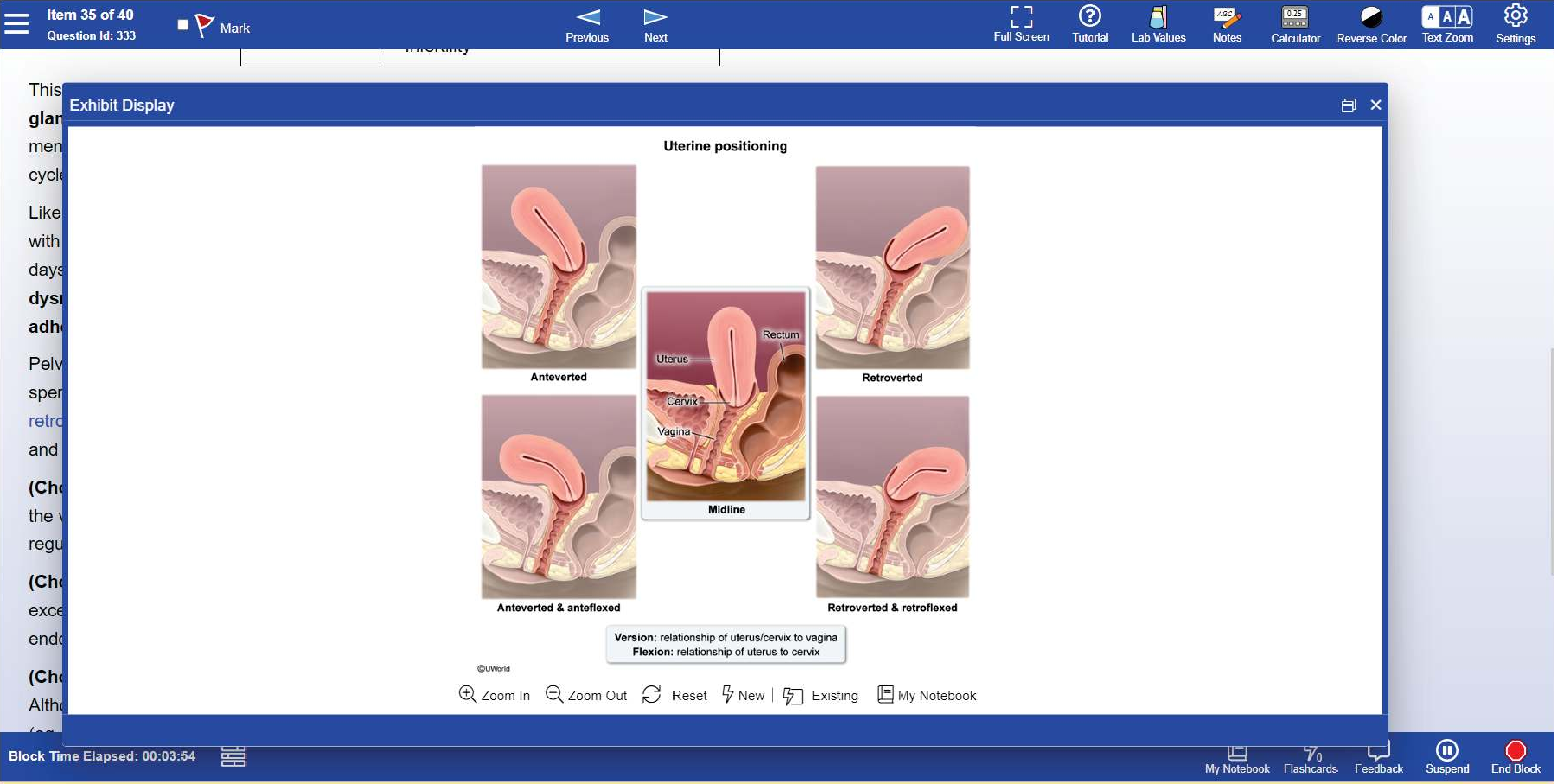
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Anteverted
Retroverted
Rectum
Uterus
Cervix
Vagina
Midline
Anteverted & anteflexed
Retroverted & retroflexed
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Uterine positioning

Version: relationship of uterus/cervix to vagina
Flexion: relationship of uterus to cervix

adhesion formation, which, in turn, distorts pelvic organ anatomy and function.

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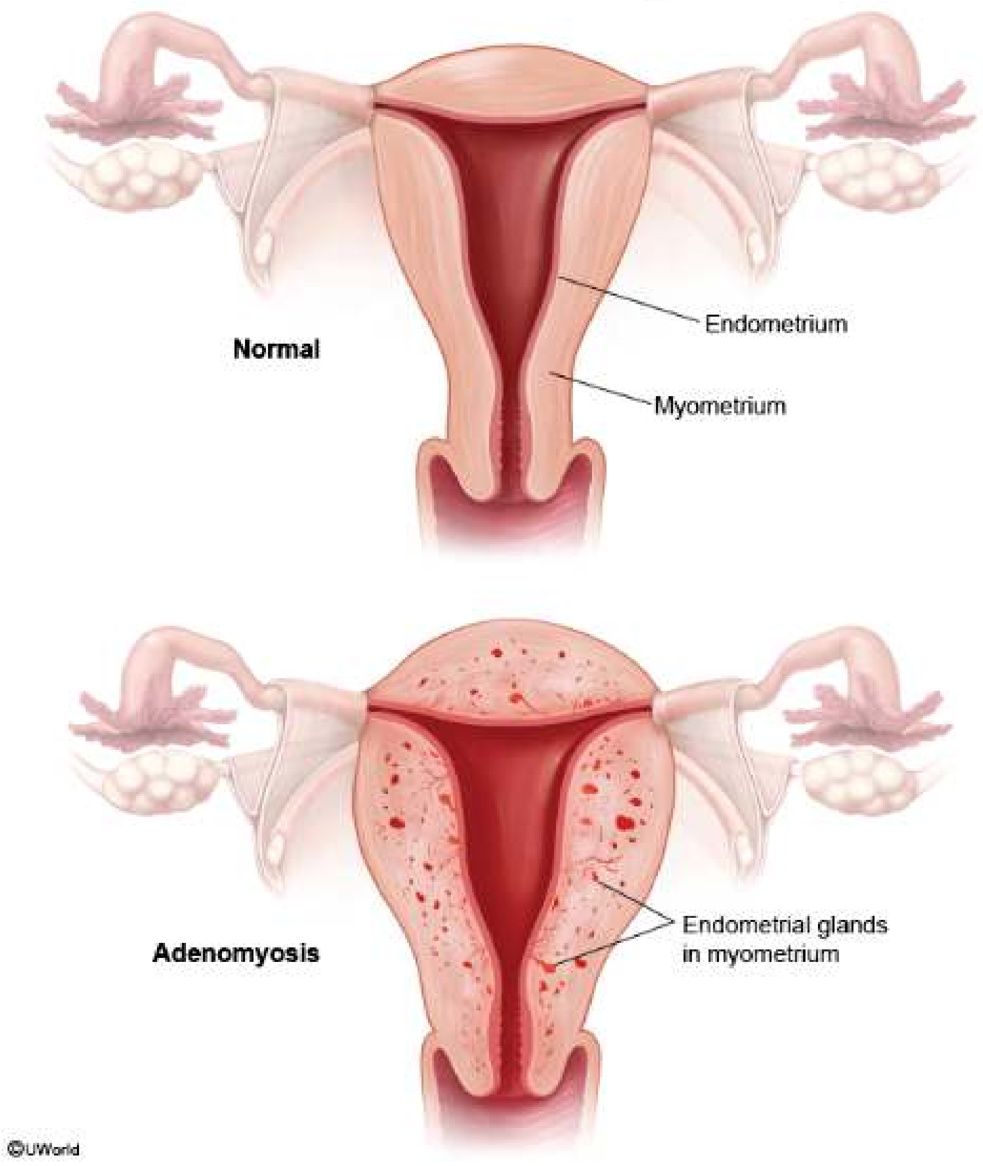
Normal uterus vs adenomyosis


Endometrium
Myometrium
Normal
Adenomyosis
Endometrial glands in myometrium
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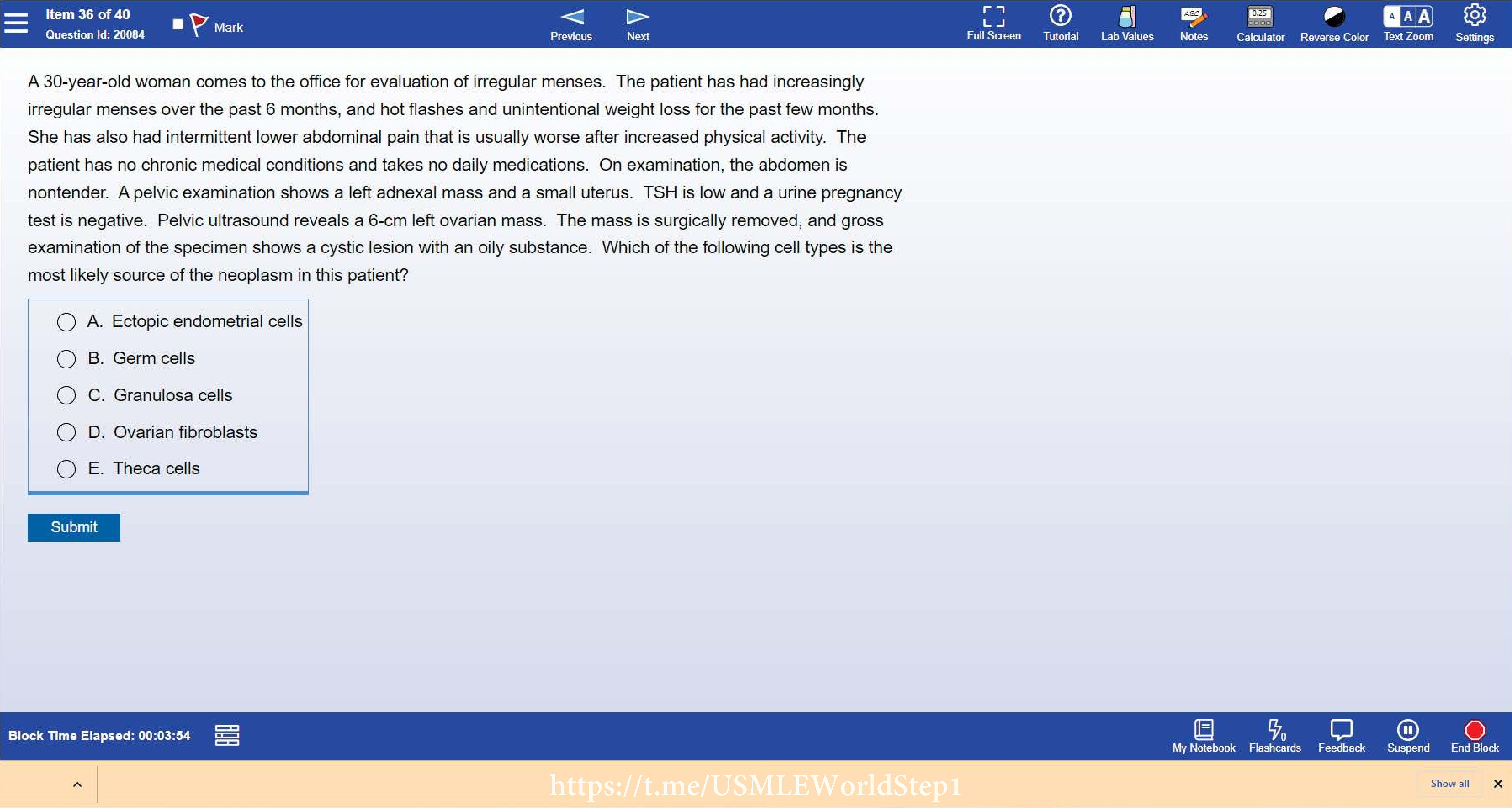
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Question Id: 20084

A 30-year-old woman comes to the office for evaluation of irregular menses. The patient has had increasingly irregular menses over the past 6 months, and hot flashes and unintentional weight loss for the past few months. She has also had intermittent lower abdominal pain that is usually worse after increased physical activity. The patient has no chronic medical conditions and takes no daily medications. On examination, the abdomen is nontender. A pelvic examination shows a left adnexal mass and a small uterus. TSH is low and a urine pregnancy test is negative. Pelvic ultrasound reveals a 6-cm left ovarian mass. The mass is surgically removed, and gross examination of the specimen shows a cystic lesion with an oily substance. Which of the following cell types is the most likely source of the neoplasm in this patient?

○ A. Ectopic endometrial cells
○ B. Germ cells
○ C. Granulosa cells
○ D. Ovarian fibroblasts
○ E. Theca cells

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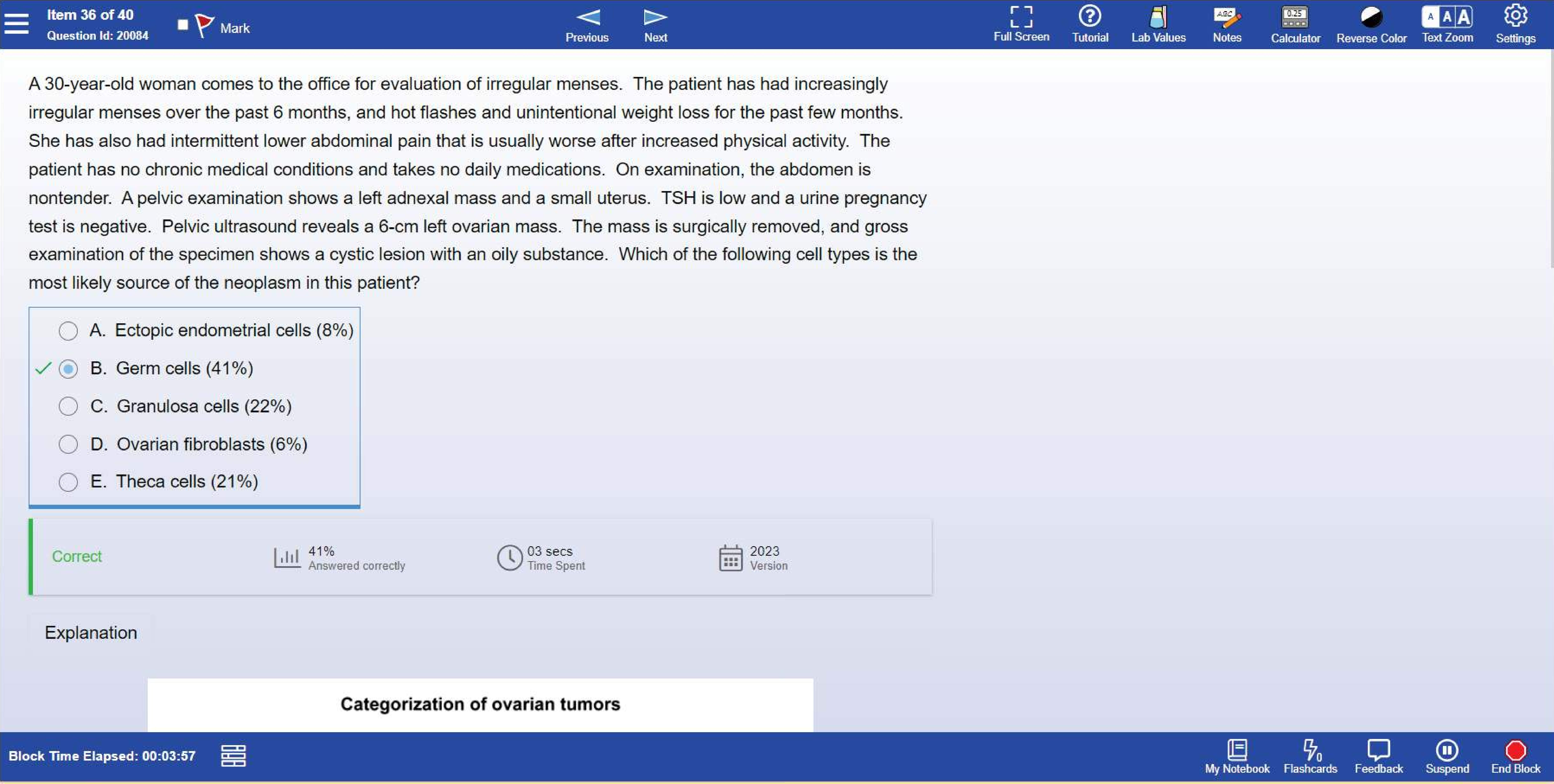
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○ A. Ectopic endometrial cells (8%)
✓ ● B. Germ cells (41%)
○ C. Granulosa cells (22%)
○ D. Ovarian fibroblasts (6%)
○ E. Theca cells (21%)

Correct

41% Answered correctly

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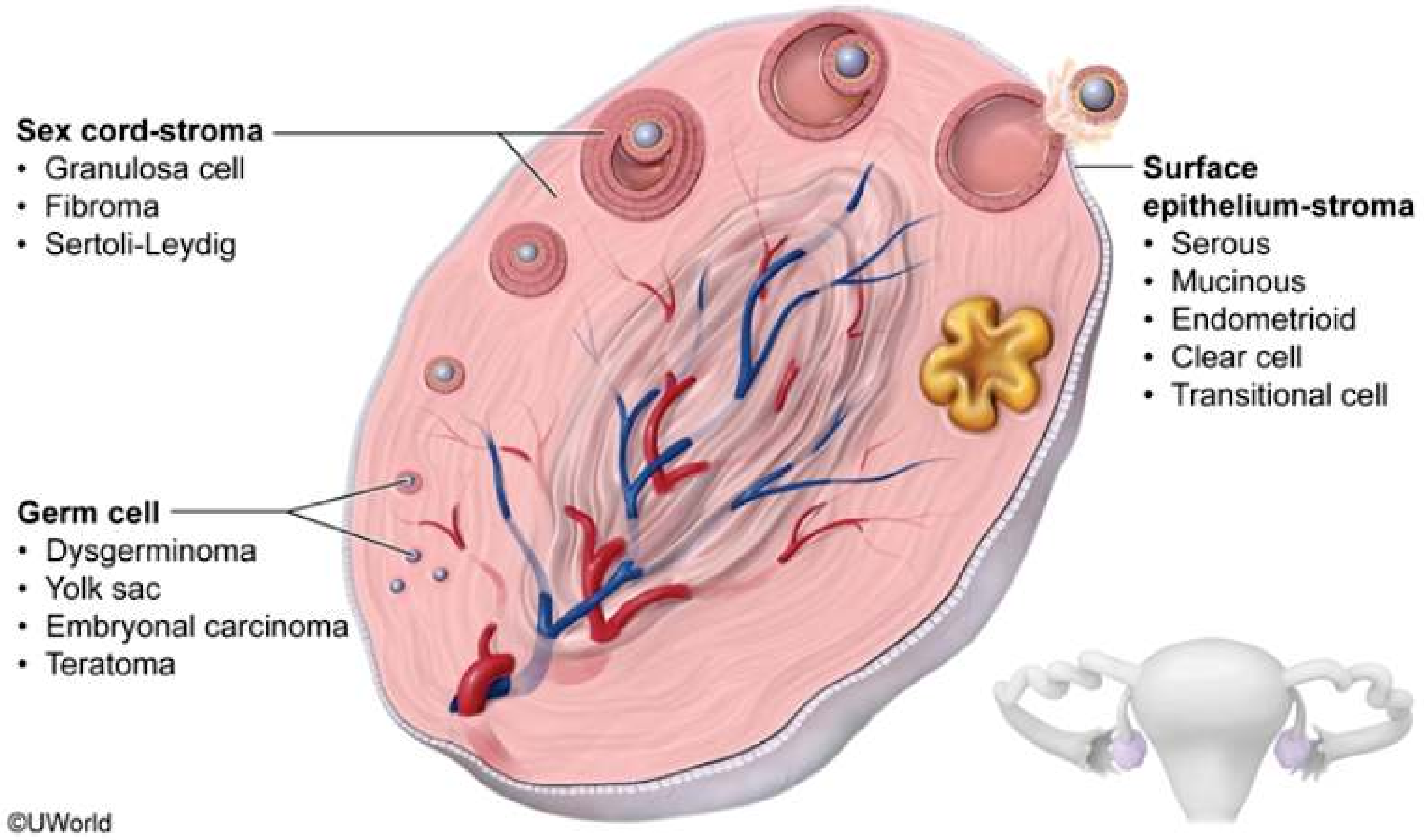
Explanation

Categorization of ovarian tumors

Explanation

Exhibit Display

Categorization of ovarian tumors


Sex cord-stroma
- Granulosa cell
- Fibroma
- Sertoli-Leydig
Surface epithelium-stroma
- Serous
- Mucinous
- Endometrioid
- Clear cell
- Transitional cell
Germ cell
- Dysgerminoma
- Yolk sac
- Embryonal carcinoma
- Teratoma
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- including estrogen (granulosa cells) and testosterone (Sertoli-Leydig cells).

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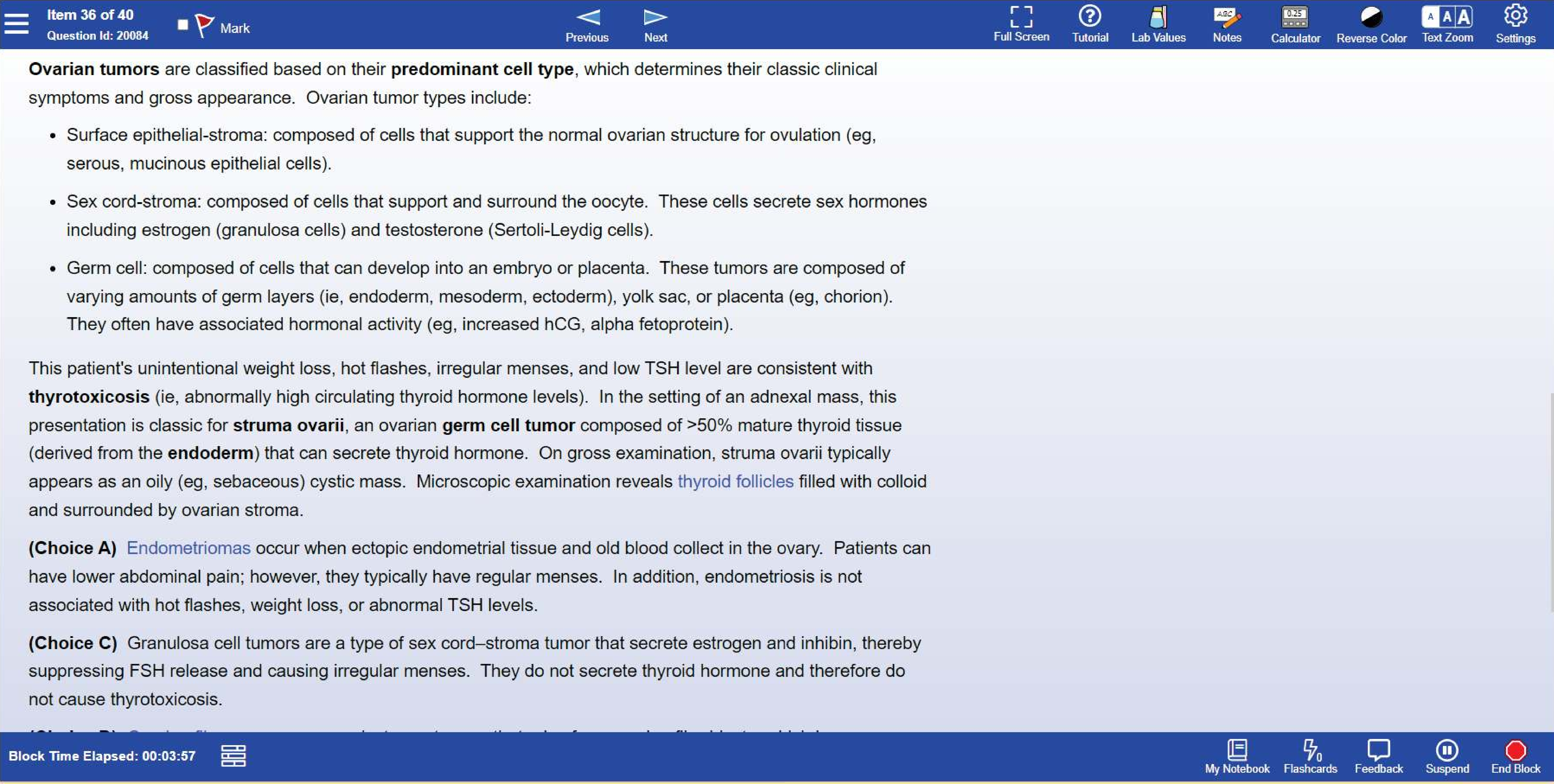
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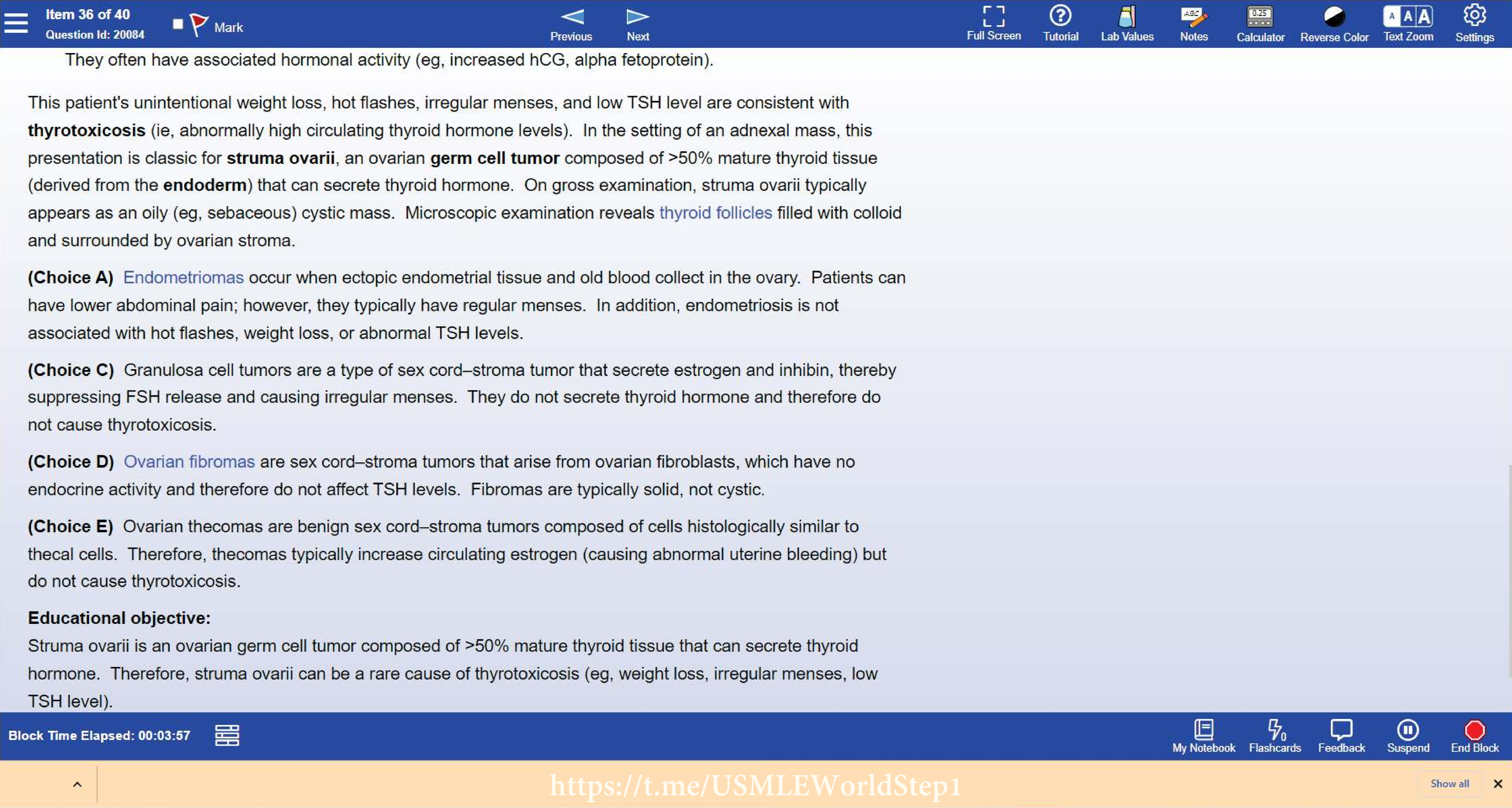
Ovarian tumors are classified based on their **predominant cell type**, which determines their classic clinical symptoms and gross appearance. Ovarian tumor types include:

- Surface epithelial-stroma: composed of cells that support the normal ovarian structure for ovulation (eg, serous, mucinous epithelial cells).
- Sex cord-stroma: composed of cells that support and surround the oocyte. These cells secrete sex hormones including estrogen (granulosa cells) and testosterone (Sertoli-Leydig cells).
- Germ cell: composed of cells that can develop into an embryo or placenta. These tumors are composed of varying amounts of germ layers (ie, endoderm, mesoderm, ectoderm), yolk sac, or placenta (eg, chorion). They often have associated hormonal activity (eg, increased hCG, alpha fetoprotein).

This patient's unintentional weight loss, hot flashes, irregular menses, and low TSH level are consistent with **thyrotoxicosis** (ie, abnormally high circulating thyroid hormone levels). In the setting of an adnexal mass, this presentation is classic for **struma ovarii**, an ovarian **germ cell tumor** composed of >50% mature thyroid tissue (derived from the **endoderm**) that can secrete thyroid hormone. On gross examination, struma ovarii typically appears as an oily (eg, sebaceous) cystic mass. Microscopic examination reveals thyroid follicles filled with colloid and surrounded by ovarian stroma.

(Choice A) Endometriomas occur when ectopic endometrial tissue and old blood collect in the ovary. Patients can have lower abdominal pain; however, they typically have regular menses. In addition, endometriosis is not associated with hot flashes, weight loss, or abnormal TSH levels.

(Choice C) Granulosa cell tumors are a type of sex cord–stroma tumor that secrete estrogen and inhibin, thereby suppressing FSH release and causing irregular menses. They do not secrete thyroid hormone and therefore do not cause thyrotoxicosis.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(Choice C) Granulosa cell tumors are a type of sex cord–stroma tumor that secrete estrogen and inhibin, thereby suppressing FSH release and causing irregular menses. They do not secrete thyroid hormone and therefore do not cause thyrotoxicosis.

(Choice D) Ovarian fibromas are sex cord–stroma tumors that arise from ovarian fibroblasts, which have no endocrine activity and therefore do not affect TSH levels. Fibromas are typically solid, not cystic.

(Choice E) Ovarian thecomas are benign sex cord–stroma tumors composed of cells histologically similar to thecal cells. Therefore, thecomas typically increase circulating estrogen (causing abnormal uterine bleeding) but do not cause thyrotoxicosis.

Educational objective:
Struma ovarii is an ovarian germ cell tumor composed of >50% mature thyroid tissue that can secrete thyroid hormone. Therefore, struma ovarii can be a rare cause of thyrotoxicosis (eg, weight loss, irregular menses, low TSH level).

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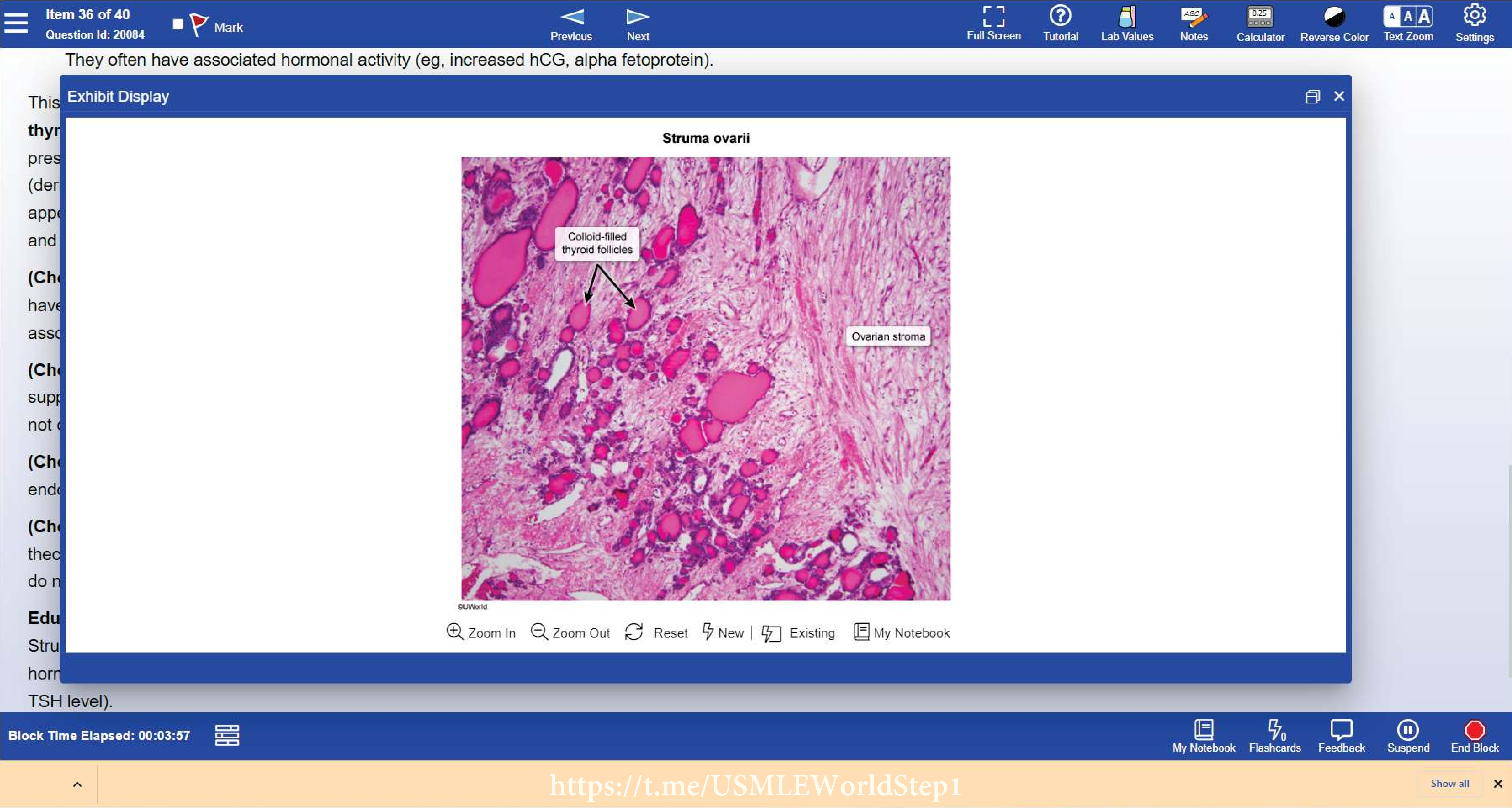
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They often have associated hormonal activity (eg, increased hCG, alpha fetoprotein).

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Struma ovarii

Colloid-filled thyroid follicles
Ovarian stroma
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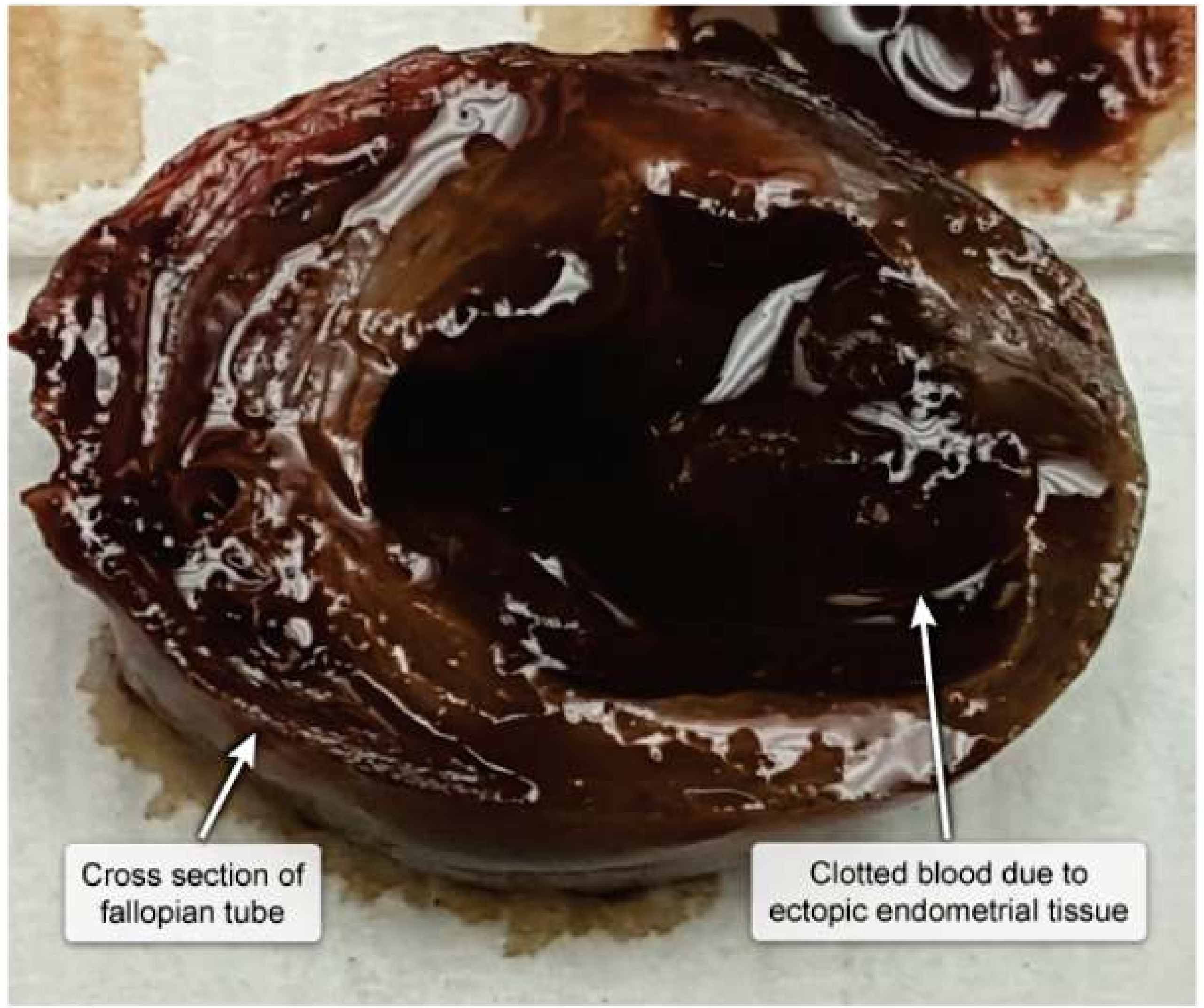
Endometriosis


Cross section of fallopian tube
Clotted blood due to ectopic endometrial tissue

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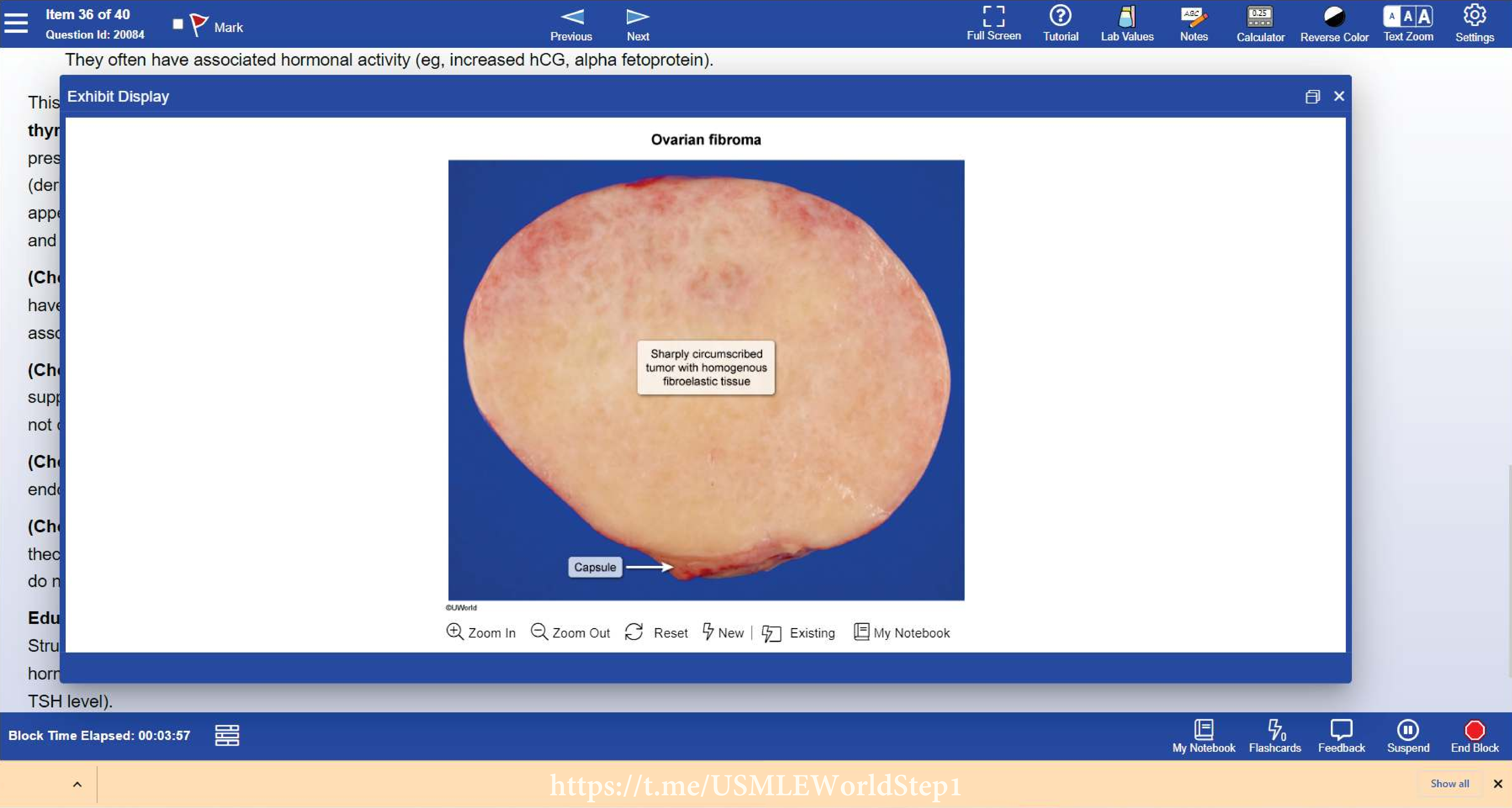
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Ovarian fibroma

Sharply circumscribed tumor with homogenous fibroelastic tissue
Capsule
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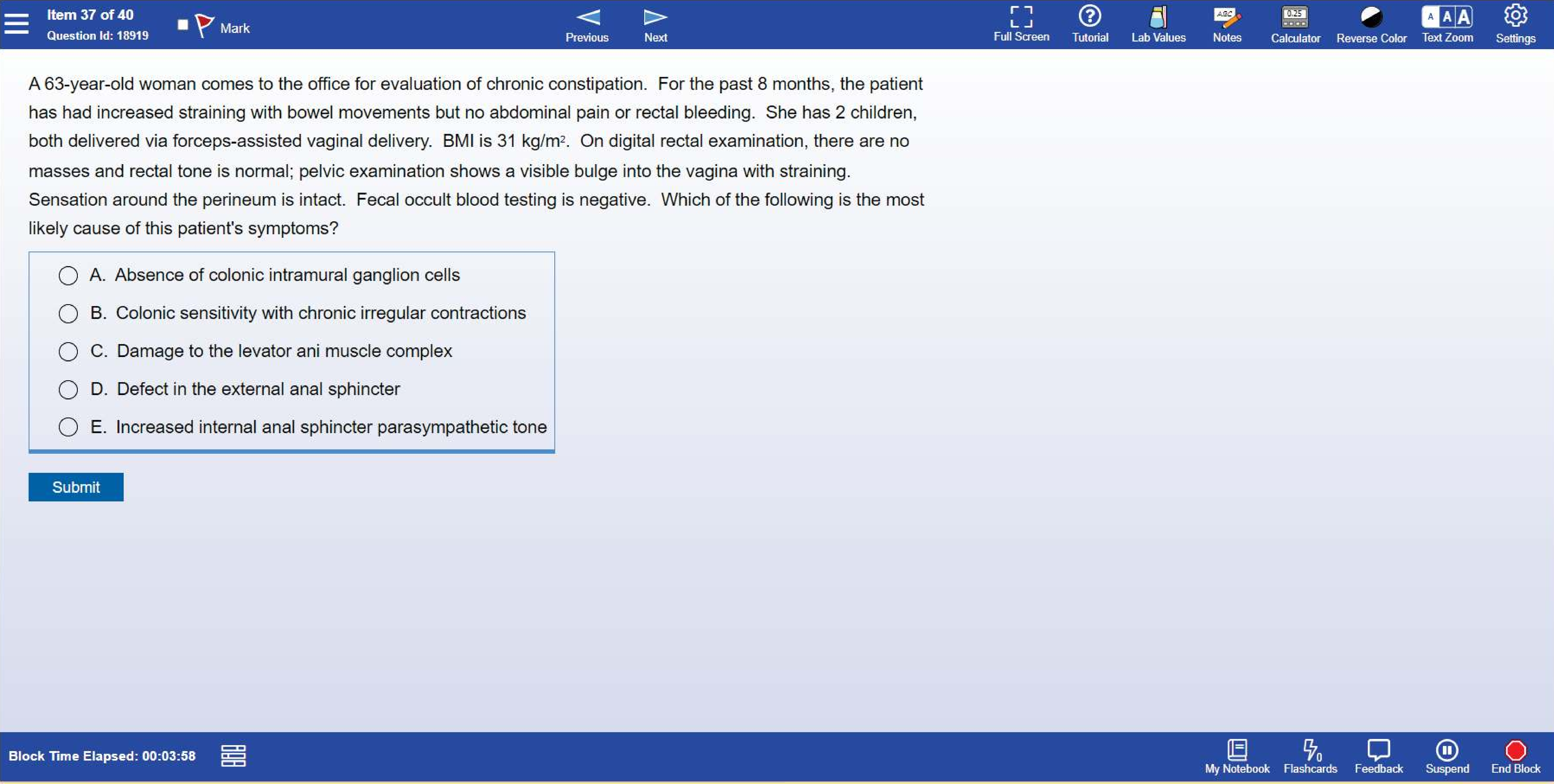
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Question Id: 18919

A 63-year-old woman comes to the office for evaluation of chronic constipation. For the past 8 months, the patient has had increased straining with bowel movements but no abdominal pain or rectal bleeding. She has 2 children, both delivered via forceps-assisted vaginal delivery. BMI is 31 kg/m^2. On digital rectal examination, there are no masses and rectal tone is normal; pelvic examination shows a visible bulge into the vagina with straining. Sensation around the perineum is intact. Fecal occult blood testing is negative. Which of the following is the most likely cause of this patient's symptoms?

○ A. Absence of colonic intramural ganglion cells
○ B. Colonic sensitivity with chronic irregular contractions
○ C. Damage to the levator ani muscle complex
○ D. Defect in the external anal sphincter
○ E. Increased internal anal sphincter parasympathetic tone

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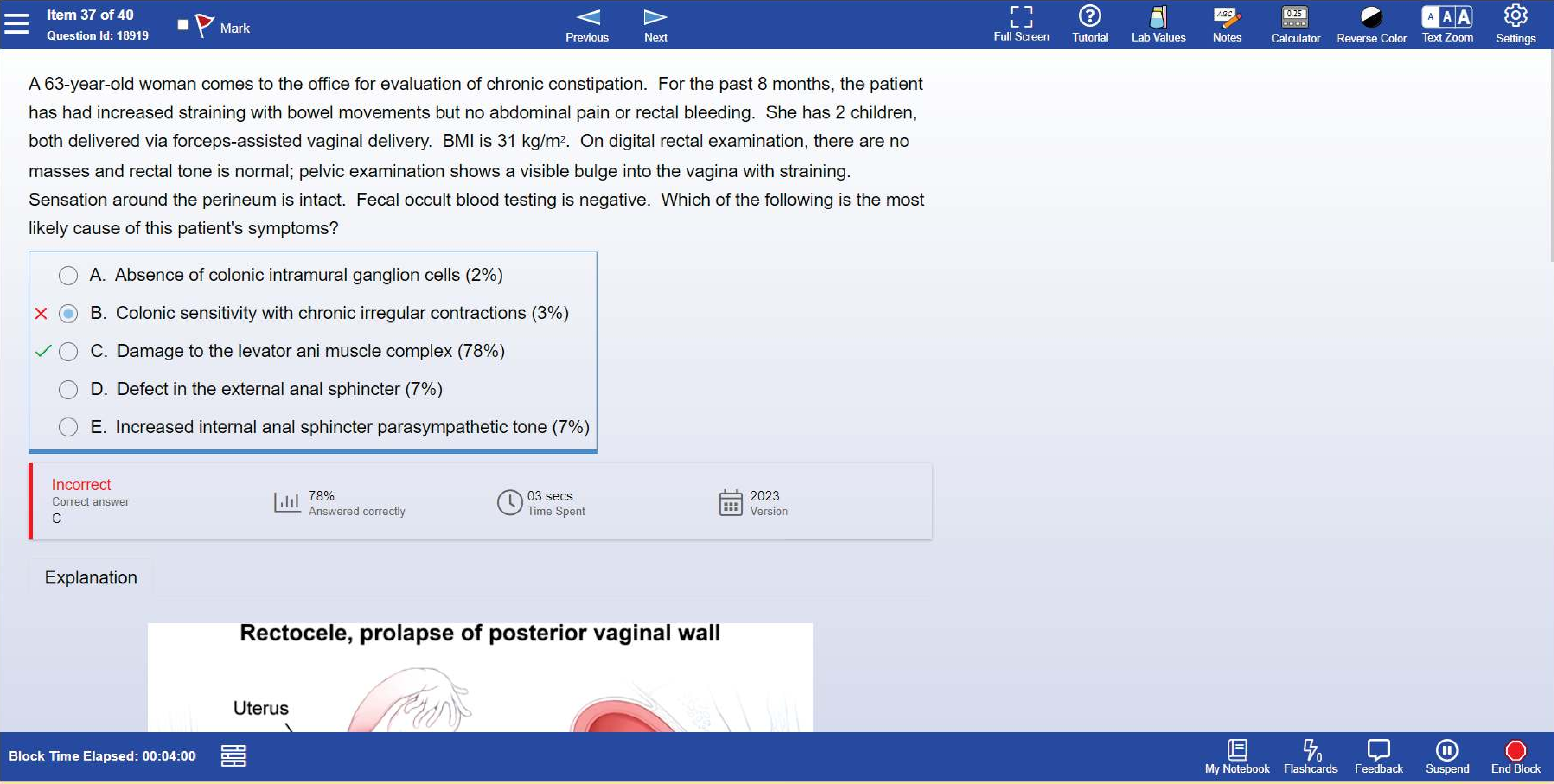
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A 63-year-old woman comes to the office for evaluation of chronic constipation. For the past 8 months, the patient has had increased straining with bowel movements but no abdominal pain or rectal bleeding. She has 2 children, both delivered via forceps-assisted vaginal delivery. BMI is 31 kg/m². On digital rectal examination, there are no masses and rectal tone is normal; pelvic examination shows a visible bulge into the vagina with straining. Sensation around the perineum is intact. Fecal occult blood testing is negative. Which of the following is the most likely cause of this patient's symptoms?

- ○ A. Absence of colonic intramural ganglion cells (2%)
- ✗ ● B. Colonic sensitivity with chronic irregular contractions (3%)
- ✓ ○ C. Damage to the levator ani muscle complex (78%)
- ○ D. Defect in the external anal sphincter (7%)
- ○ E. Increased internal anal sphincter parasympathetic tone (7%)

Incorrect
Correct answer
C

78%
Answered correctly

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Explanation

Rectocele, prolapse of posterior vaginal wall

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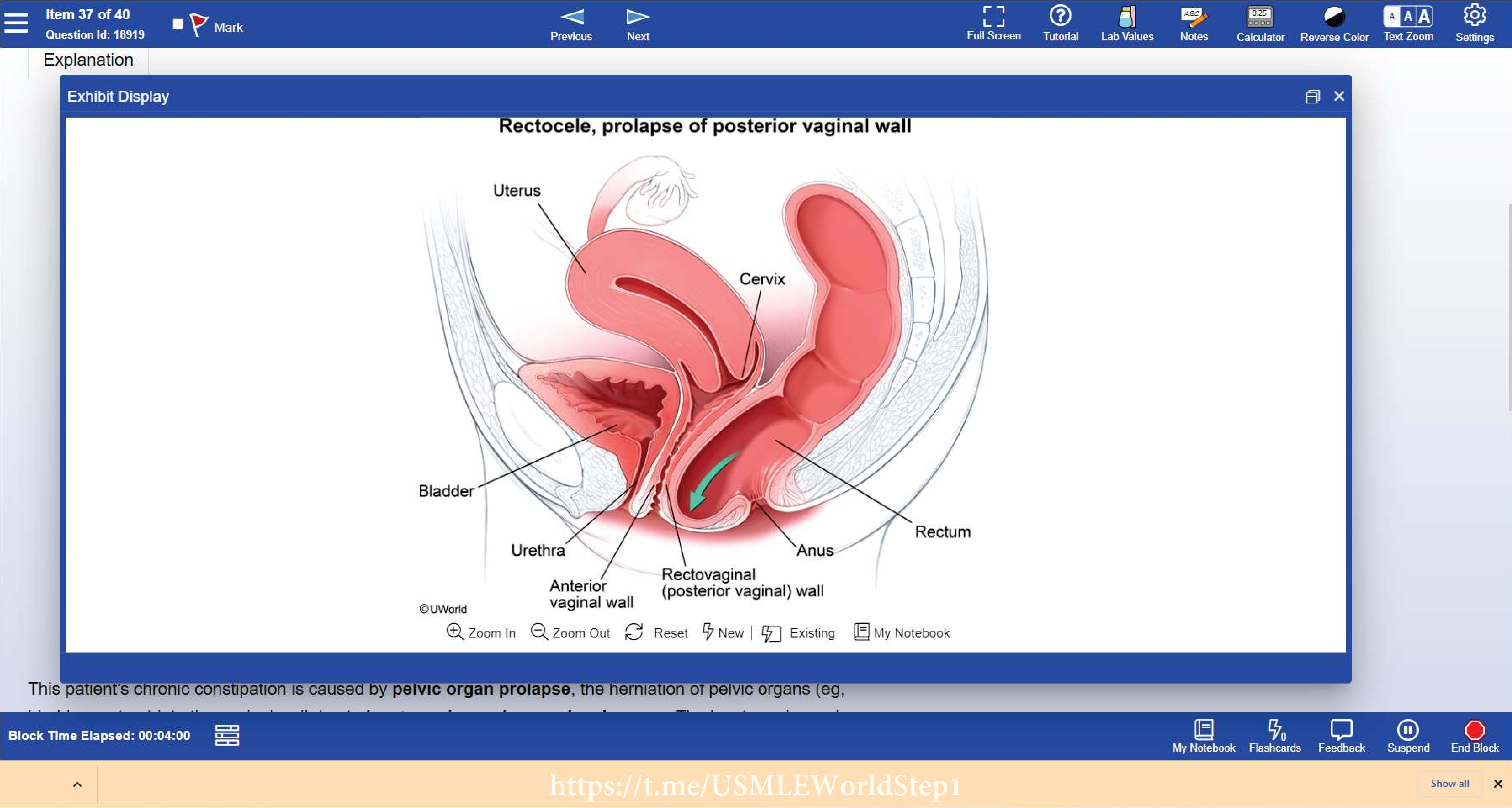
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Uterus
Cervix
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Rectum
Urethra
Anus
Anterior vaginal wall
Rectovaginal (posterior vaginal) wall
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Rectocele, prolapse of posterior vaginal wall

This patient's chronic constipation is caused by **pelvic organ prolapse**, the herniation of pelvic organs (eg,

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This patient's chronic constipation is caused by **pelvic organ prolapse**, the herniation of pelvic organs (eg, bladder, rectum) into the vaginal wall due to **levator ani muscle complex damage**. The levator ani muscle complex forms most of the pelvic floor and functions to hold the pelvic organs in a stable position; when this complex is damaged, such as with increased intraabdominal pressure (eg, **pregnancy**, obesity) or obstetric trauma (eg, forceps-assisted vaginal delivery), there is increased pelvic floor laxity, resulting in decreased pelvic organ support.

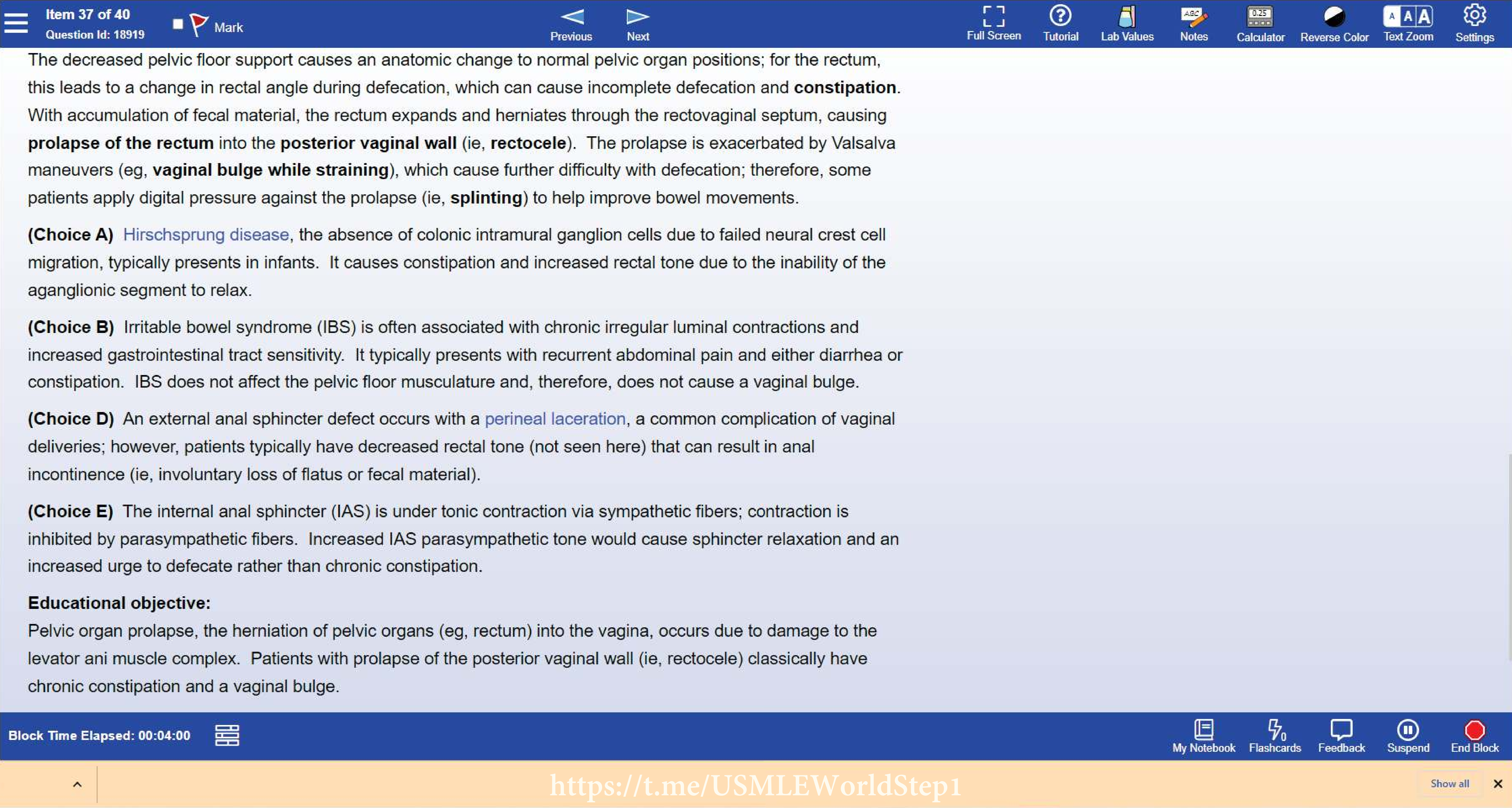
The decreased pelvic floor support causes an anatomic change to normal pelvic organ positions; for the rectum, this leads to a change in rectal angle during defecation, which can cause incomplete defecation and **constipation**. With accumulation of fecal material, the rectum expands and herniates through the rectovaginal septum, causing **prolapse of the rectum** into the **posterior vaginal wall** (ie, **rectocele**). The prolapse is exacerbated by Valsalva maneuvers (eg, **vaginal bulge while straining**), which cause further difficulty with defecation; therefore, some patients apply digital pressure against the prolapse (ie, **splinting**) to help improve bowel movements.

(Choice A) Hirschsprung disease, the absence of colonic intramural ganglion cells due to failed neural crest cell migration, typically presents in infants. It causes constipation and increased rectal tone due to the inability of the aganglionic segment to relax.

(Choice B) Irritable bowel syndrome (IBS) is often associated with chronic irregular luminal contractions and increased gastrointestinal tract sensitivity. It typically presents with recurrent abdominal pain and either diarrhea or constipation. IBS does not affect the pelvic floor musculature and, therefore, does not cause a vaginal bulge.

(Choice D) An external anal sphincter defect occurs with a perineal laceration, a common complication of vaginal deliveries; however, patients typically have decreased rectal tone (not seen here) that can result in anal incontinence (ie, involuntary loss of flatus or fecal material).

(Choice E) The internal anal sphincter (IAS) is under tonic contraction via sympathetic fibers; contraction is



The decreased pelvic floor support causes an anatomic change to normal pelvic organ positions; for the rectum, this leads to a change in rectal angle during defecation, which can cause incomplete defecation and **constipation**. With accumulation of fecal material, the rectum expands and herniates through the rectovaginal septum, causing **prolapse of the rectum** into the **posterior vaginal wall** (ie, **rectocele**). The prolapse is exacerbated by Valsalva maneuvers (eg, **vaginal bulge while straining**), which cause further difficulty with defecation; therefore, some patients apply digital pressure against the prolapse (ie, **splinting**) to help improve bowel movements.

(Choice A) Hirschsprung disease, the absence of colonic intramural ganglion cells due to failed neural crest cell migration, typically presents in infants. It causes constipation and increased rectal tone due to the inability of the aganglionic segment to relax.

(Choice B) Irritable bowel syndrome (IBS) is often associated with chronic irregular luminal contractions and increased gastrointestinal tract sensitivity. It typically presents with recurrent abdominal pain and either diarrhea or constipation. IBS does not affect the pelvic floor musculature and, therefore, does not cause a vaginal bulge.

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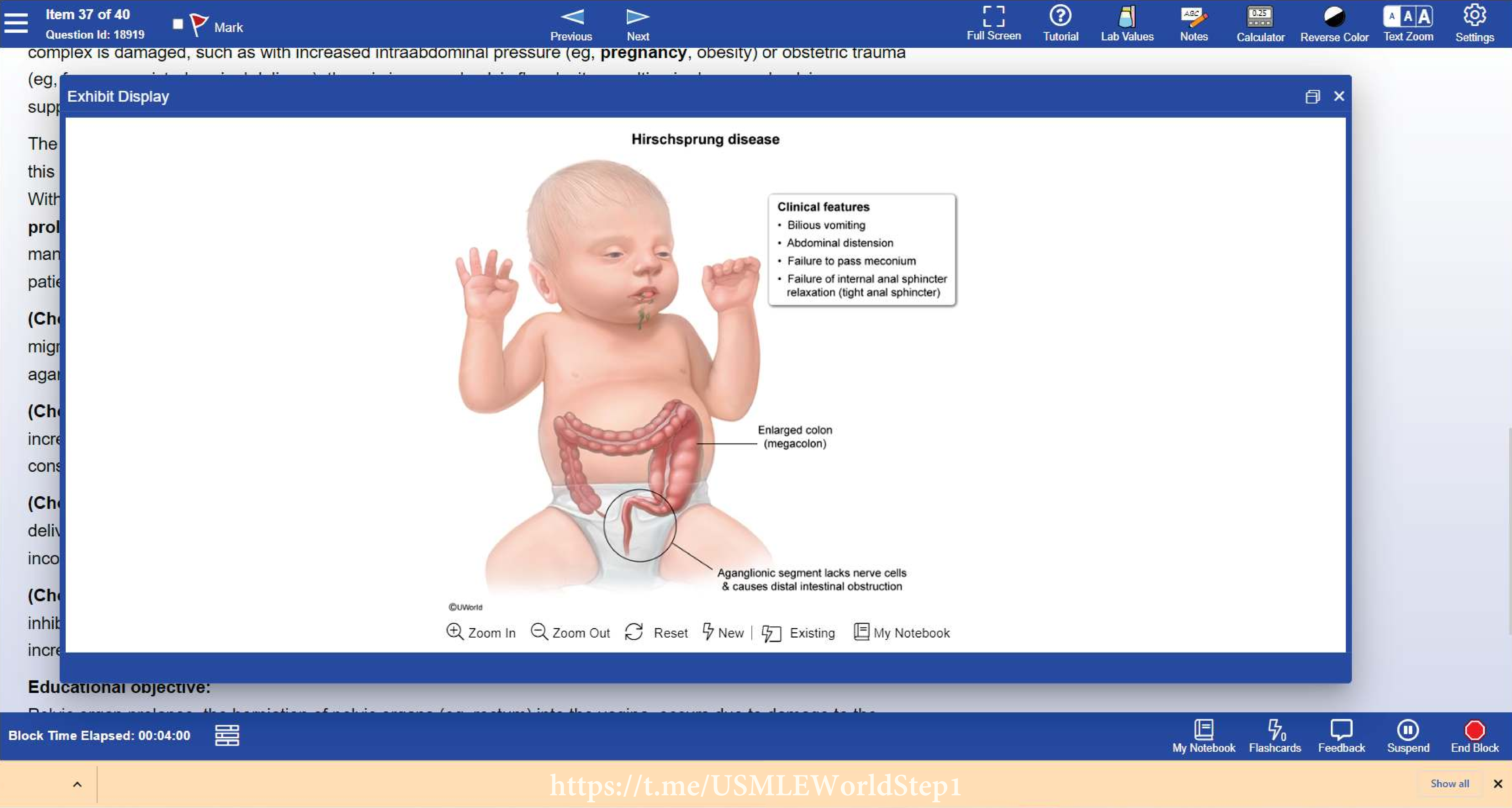
(Choice E) The internal anal sphincter (IAS) is under tonic contraction via sympathetic fibers; contraction is inhibited by parasympathetic fibers. Increased IAS parasympathetic tone would cause sphincter relaxation and an increased urge to defecate rather than chronic constipation.

Educational objective:

Pelvic organ prolapse, the herniation of pelvic organs (eg, rectum) into the vagina, occurs due to damage to the levator ani muscle complex. Patients with prolapse of the posterior vaginal wall (ie, rectocele) classically have chronic constipation and a vaginal bulge.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complex is damaged, such as with increased intraabdominal pressure (eg, **pregnancy**, obesity) or obstetric trauma

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Educational objective:

Hirschsprung disease

Clinical features
- Bilious vomiting
- Abdominal distension
- Failure to pass meconium
- Failure of internal anal sphincter relaxation (tight anal sphincter)

Enlarged colon (megacolon)
Aganglionic segment lacks nerve cells & causes distal intestinal obstruction
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complex is damaged, such as with increased intraabdominal pressure (eg, **pregnancy**, obesity) or obstetric trauma

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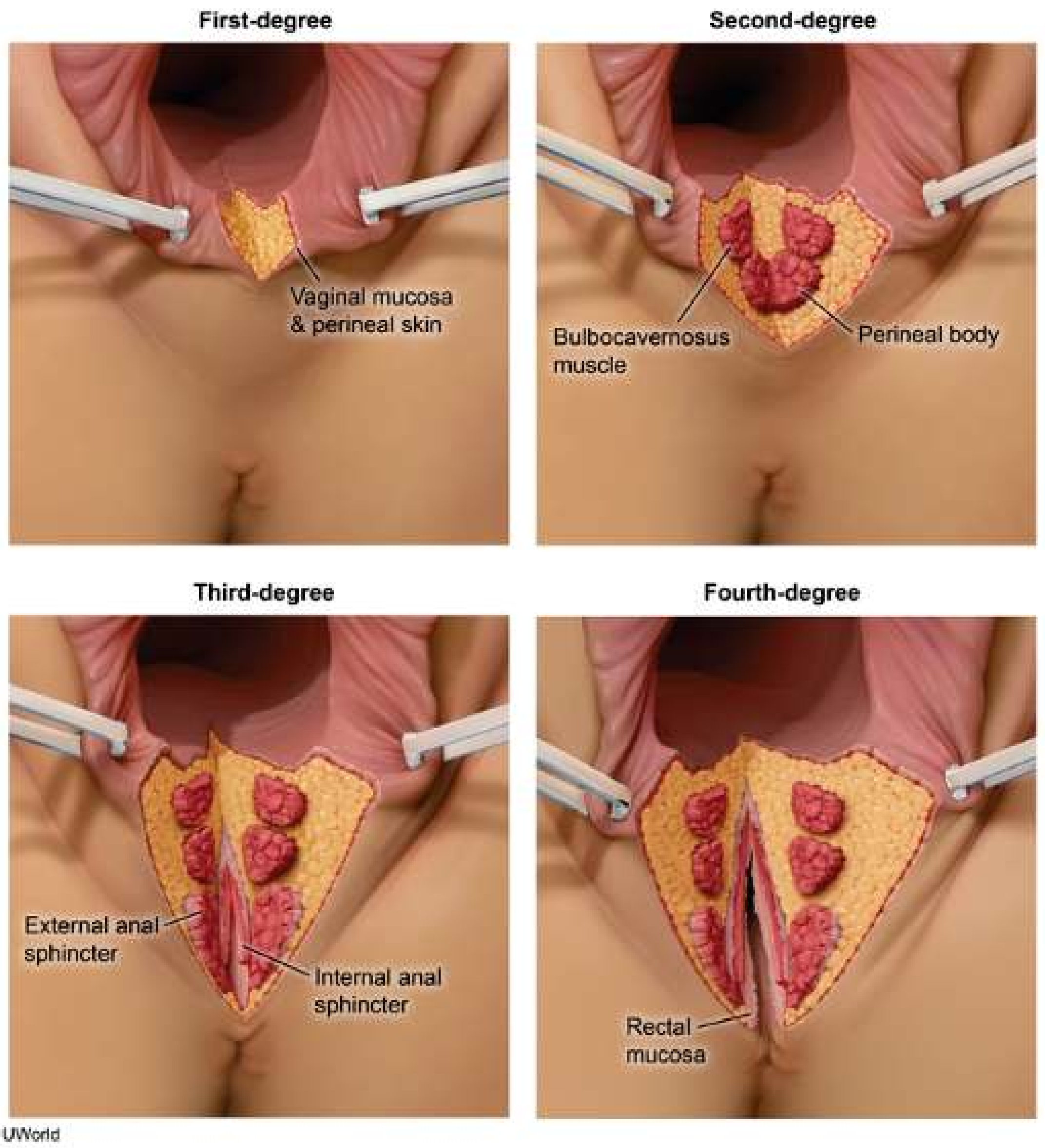

Perineal lacerations

First-degree
Vaginal mucosa & perineal skin
Second-degree
Bulbocavernosus muscle
Perineal body
Third-degree
External anal sphincter
Internal anal sphincter
Fourth-degree
Rectal mucosa
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Educational objective:

Pelvic organ prolapse, the herniation of pelvic organs (eg, rectum) into the vagina, occurs due to damage to the

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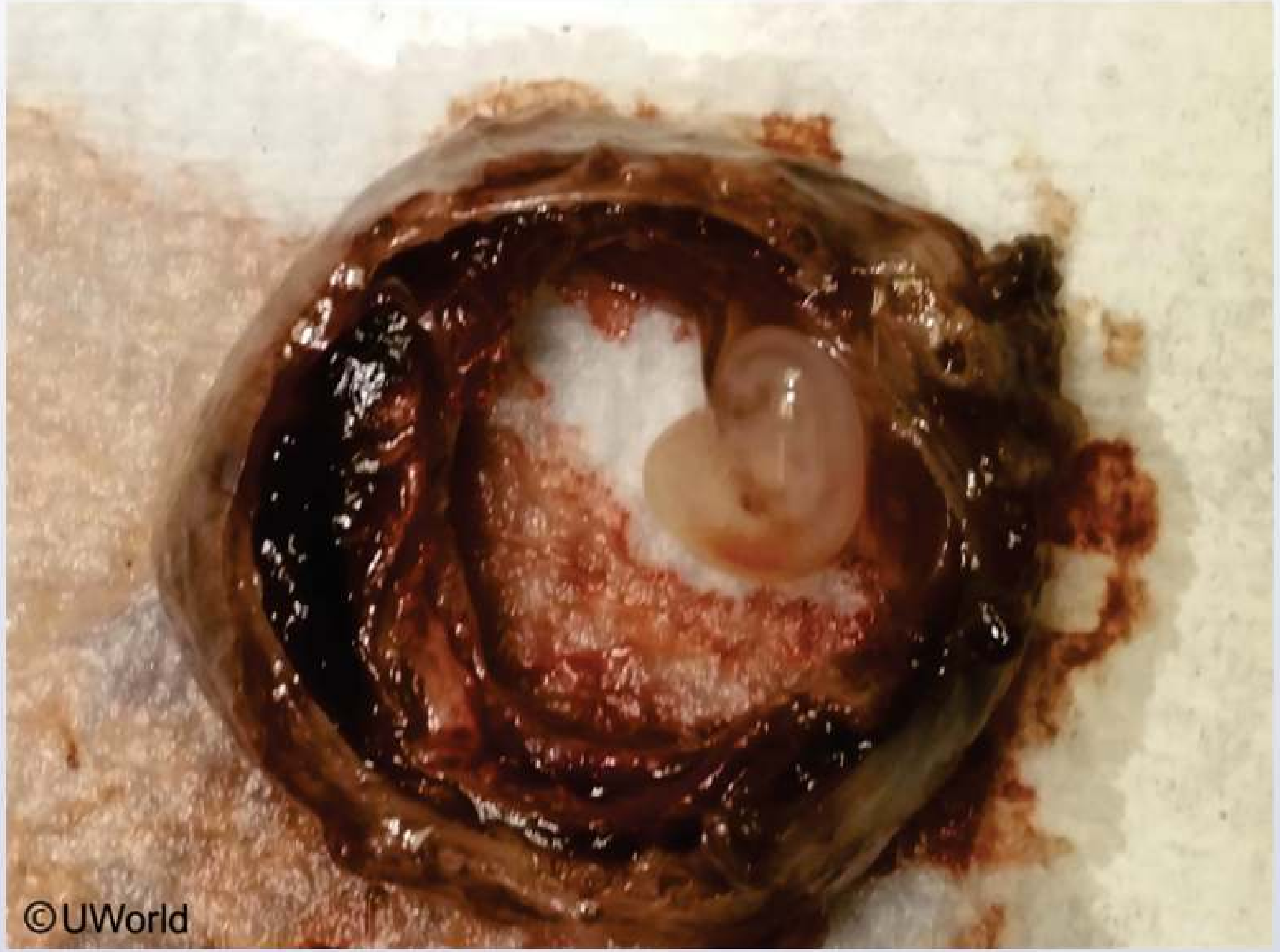
A 38-year-old woman comes to the emergency department for lower abdominal pain. The patient has had some mild, cramping abdominal pain for the past few days, but today it became constant. She has also had intermittent vaginal bleeding. The patient has a history of irregular menses, and her last menstrual period was 8 weeks ago. Physical examination shows a left adnexal mass. The patient undergoes surgery and the resected specimen is shown in the image below:



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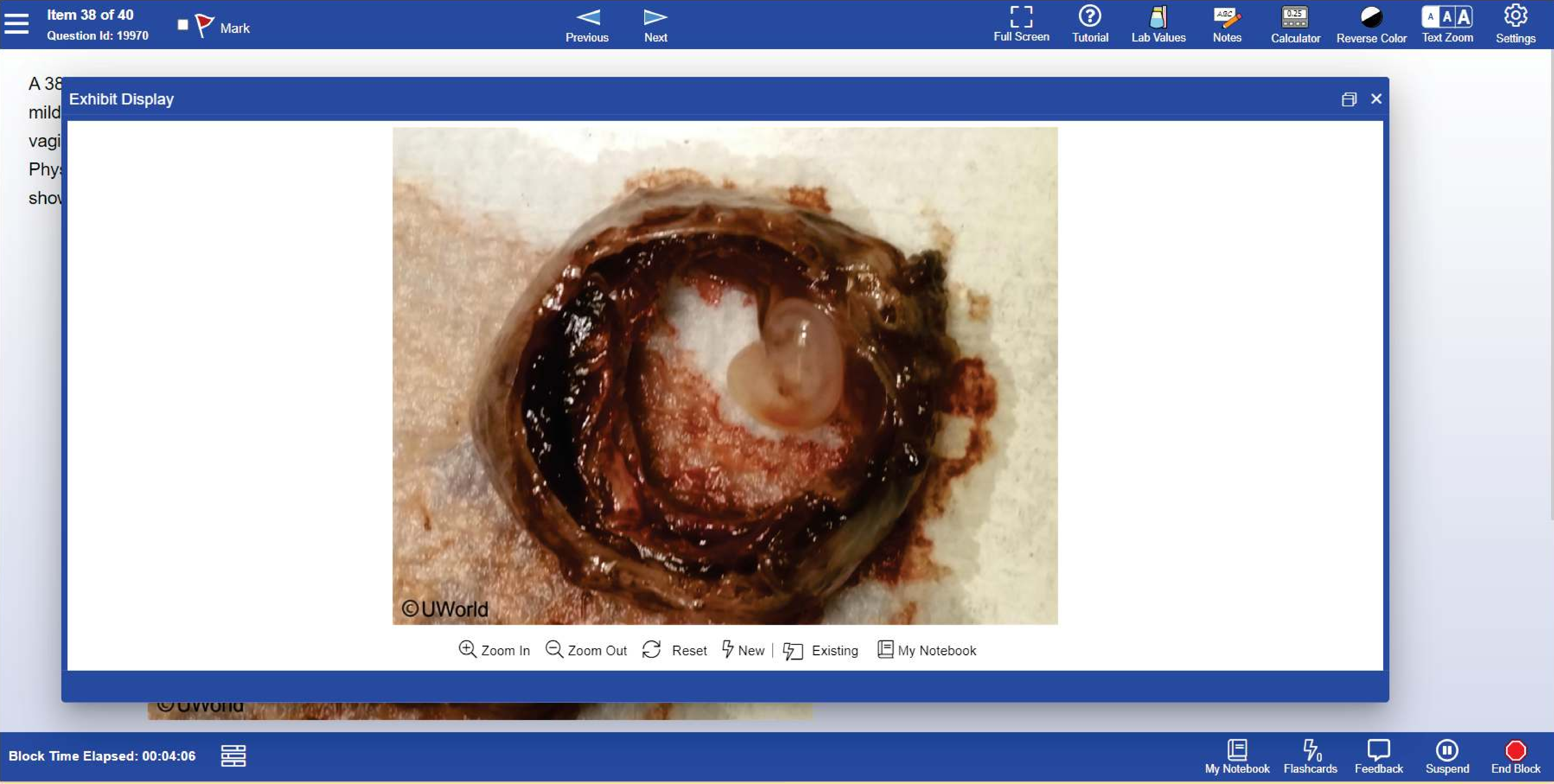

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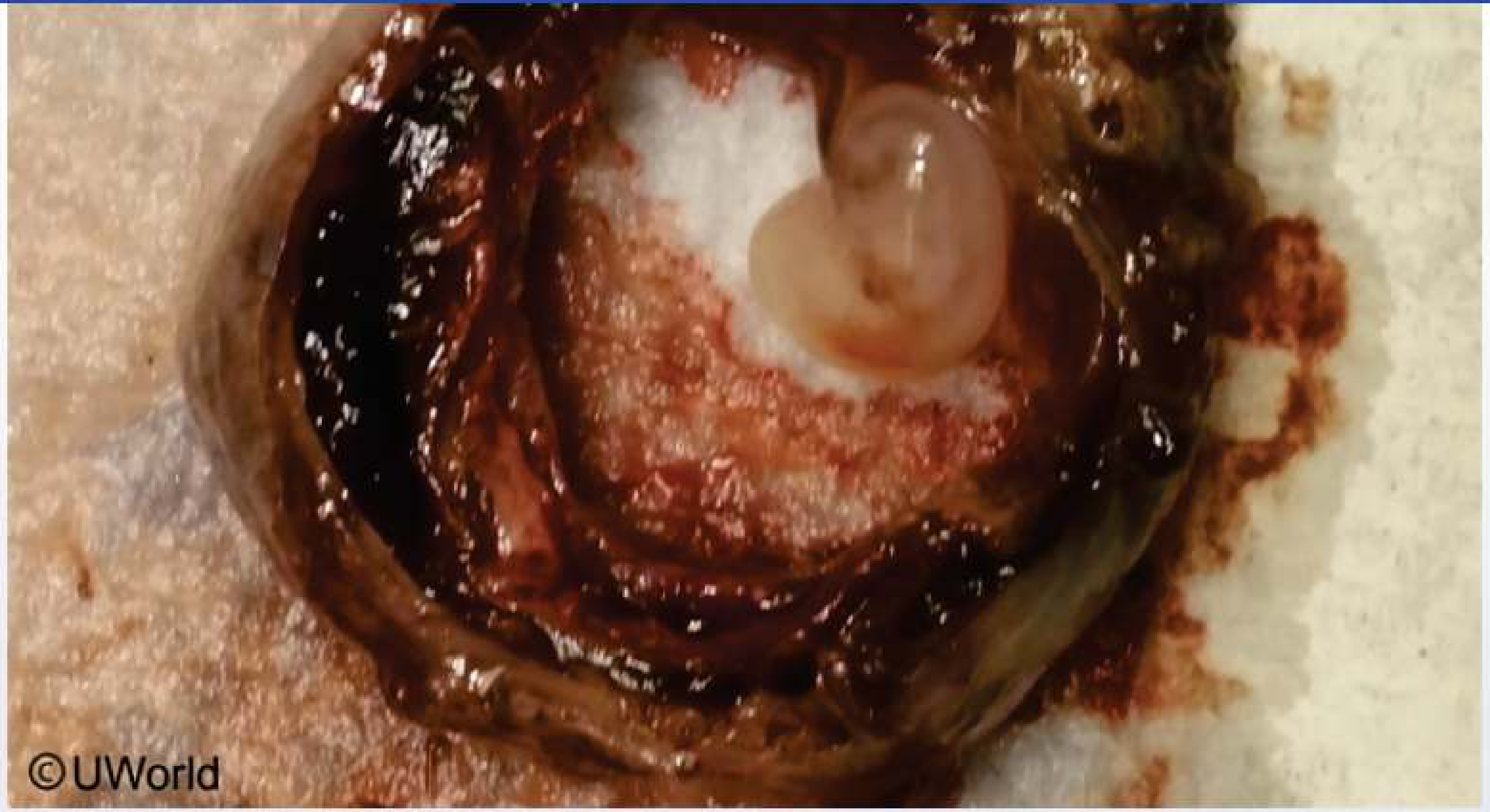

Which of the following risk factors is most strongly associated with this patient's condition?

○ A. Family history of ovarian cancer
○ B. Müllerian anomaly
○ C. Prior pelvic surgery
○ D. Progestin-only oral contraceptive use
○ E. Recent anticoagulant use

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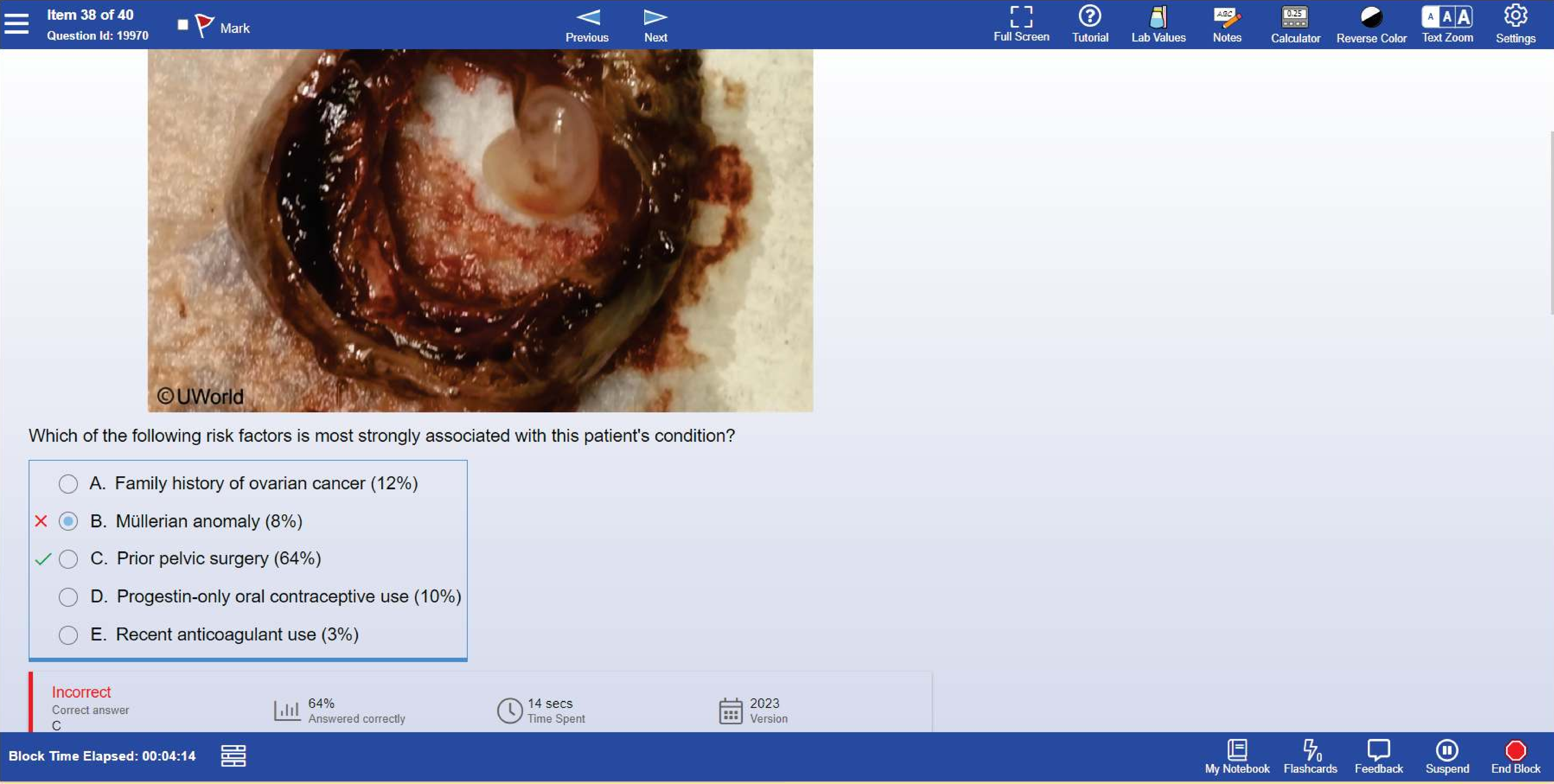
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Which of the following risk factors is most strongly associated with this patient's condition?

- ○ A. Family history of ovarian cancer (12%)
- ✗ ● B. Müllerian anomaly (8%)
- ✓ ○ C. Prior pelvic surgery (64%)
- ○ D. Progestin-only oral contraceptive use (10%)
- ○ E. Recent anticoagulant use (3%)

Incorrect
Correct answer
C

64%
Answered correctly

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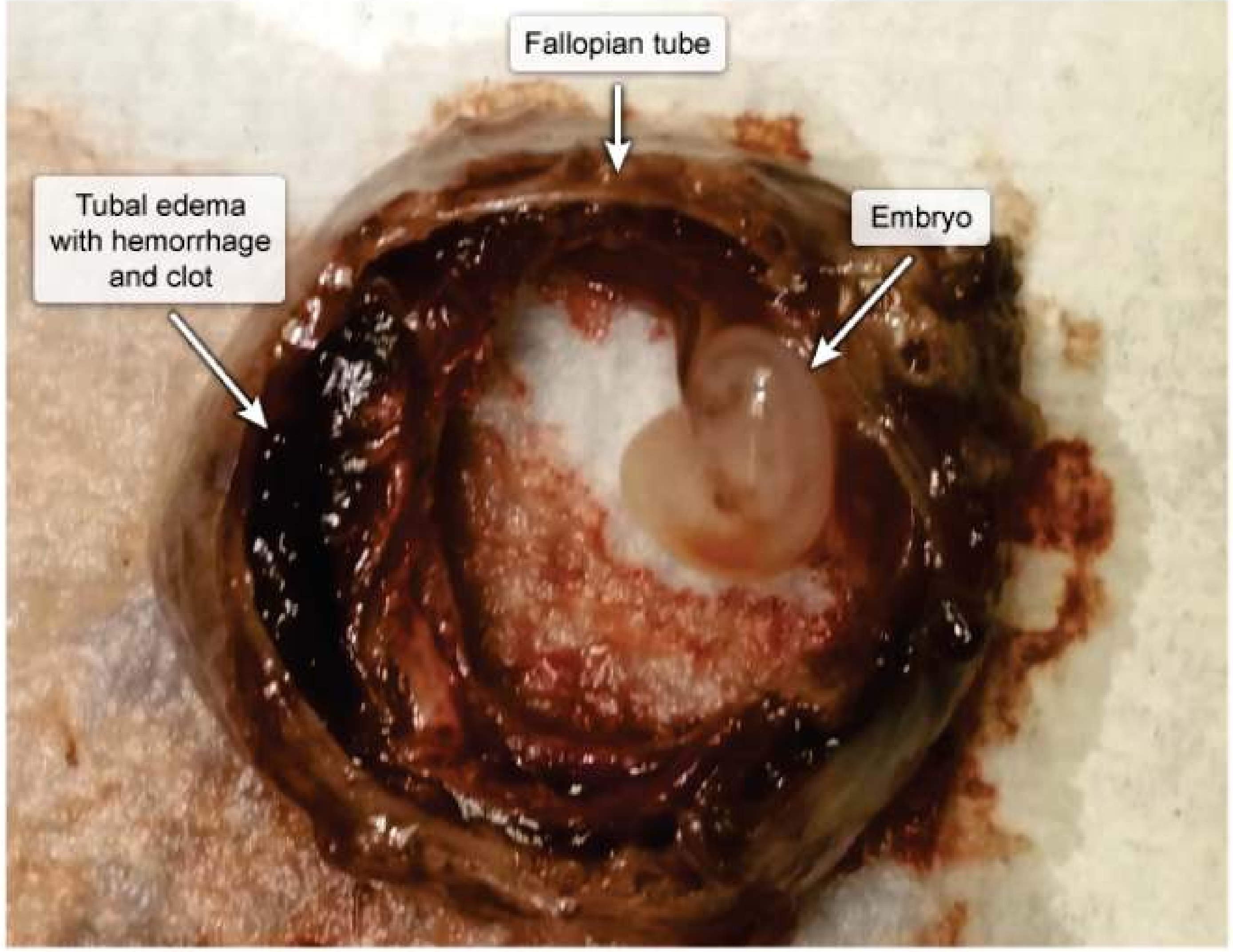
Ectopic pregnancy


Fallopian tube
Tubal edema with hemorrhage and clot
Embryo

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pregnancy (ie, embryo implantation in an extrauterine location [most commonly the **fallopian tube**]). The surgical

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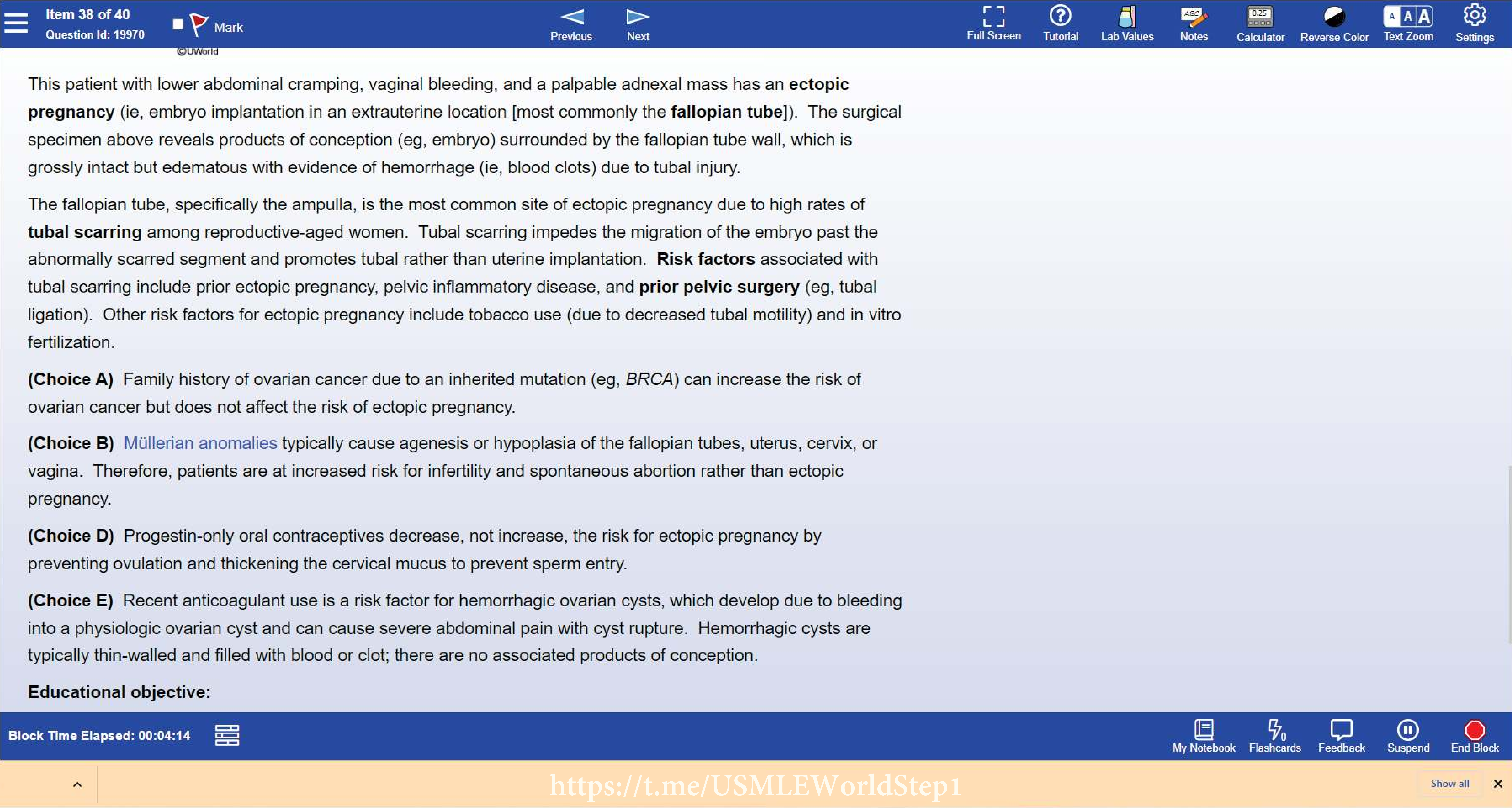
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This patient with lower abdominal cramping, vaginal bleeding, and a palpable adnexal mass has an **ectopic pregnancy** (ie, embryo implantation in an extrauterine location [most commonly the **fallopian tube**]). The surgical specimen above reveals products of conception (eg, embryo) surrounded by the fallopian tube wall, which is grossly intact but edematous with evidence of hemorrhage (ie, blood clots) due to tubal injury.

The fallopian tube, specifically the ampulla, is the most common site of ectopic pregnancy due to high rates of **tubal scarring** among reproductive-aged women. Tubal scarring impedes the migration of the embryo past the abnormally scarred segment and promotes tubal rather than uterine implantation. **Risk factors** associated with tubal scarring include prior ectopic pregnancy, pelvic inflammatory disease, and **prior pelvic surgery** (eg, tubal ligation). Other risk factors for ectopic pregnancy include tobacco use (due to decreased tubal motility) and in vitro fertilization.

(Choice A) Family history of ovarian cancer due to an inherited mutation (eg, *BRCA*) can increase the risk of ovarian cancer but does not affect the risk of ectopic pregnancy.

(Choice B) Müllerian anomalies typically cause agenesis or hypoplasia of the fallopian tubes, uterus, cervix, or vagina. Therefore, patients are at increased risk for infertility and spontaneous abortion rather than ectopic pregnancy.

(Choice D) Progestin-only oral contraceptives decrease, not increase, the risk for ectopic pregnancy by preventing ovulation and thickening the cervical mucus to prevent sperm entry.

(Choice E) Recent anticoagulant use is a risk factor for hemorrhagic ovarian cysts, which develop due to bleeding into a physiologic ovarian cyst and can cause severe abdominal pain with cyst rupture. Hemorrhagic cysts are typically thin-walled and filled with blood or clot; there are no associated products of conception.

Educational objective:

specimen above reveals products of conception (eg, embryo) surrounded by the fallopian tube wall, which is grossly intact but edematous with evidence of hemorrhage (ie, blood clots) due to tubal injury.

The fallopian tube, specifically the ampulla, is the most common site of ectopic pregnancy due to high rates of **tubal scarring** among reproductive-aged women. Tubal scarring impedes the migration of the embryo past the abnormally scarred segment and promotes tubal rather than uterine implantation. **Risk factors** associated with tubal scarring include prior ectopic pregnancy, pelvic inflammatory disease, and **prior pelvic surgery** (eg, tubal ligation). Other risk factors for ectopic pregnancy include tobacco use (due to decreased tubal motility) and in vitro fertilization.

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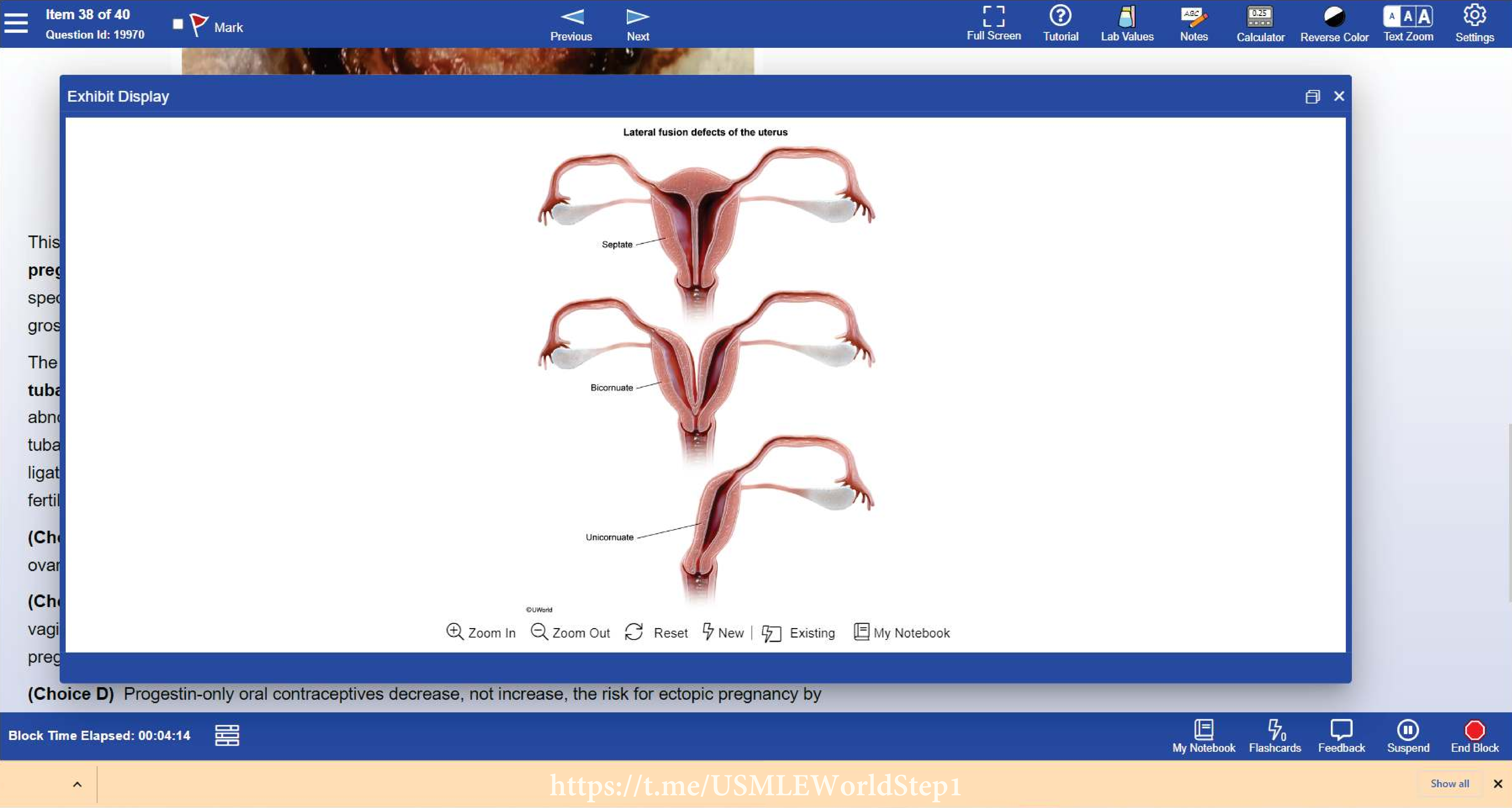
Educational objective:

Ectopic pregnancy occurs when the embryo implants in an extrauterine location, most commonly the fallopian tube. Risk factors for ectopic pregnancy include tubal scarring (eg, prior pelvic surgery, pelvic inflammatory disease), tobacco use, and in vitro fertilization.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Lateral fusion defects of the uterus

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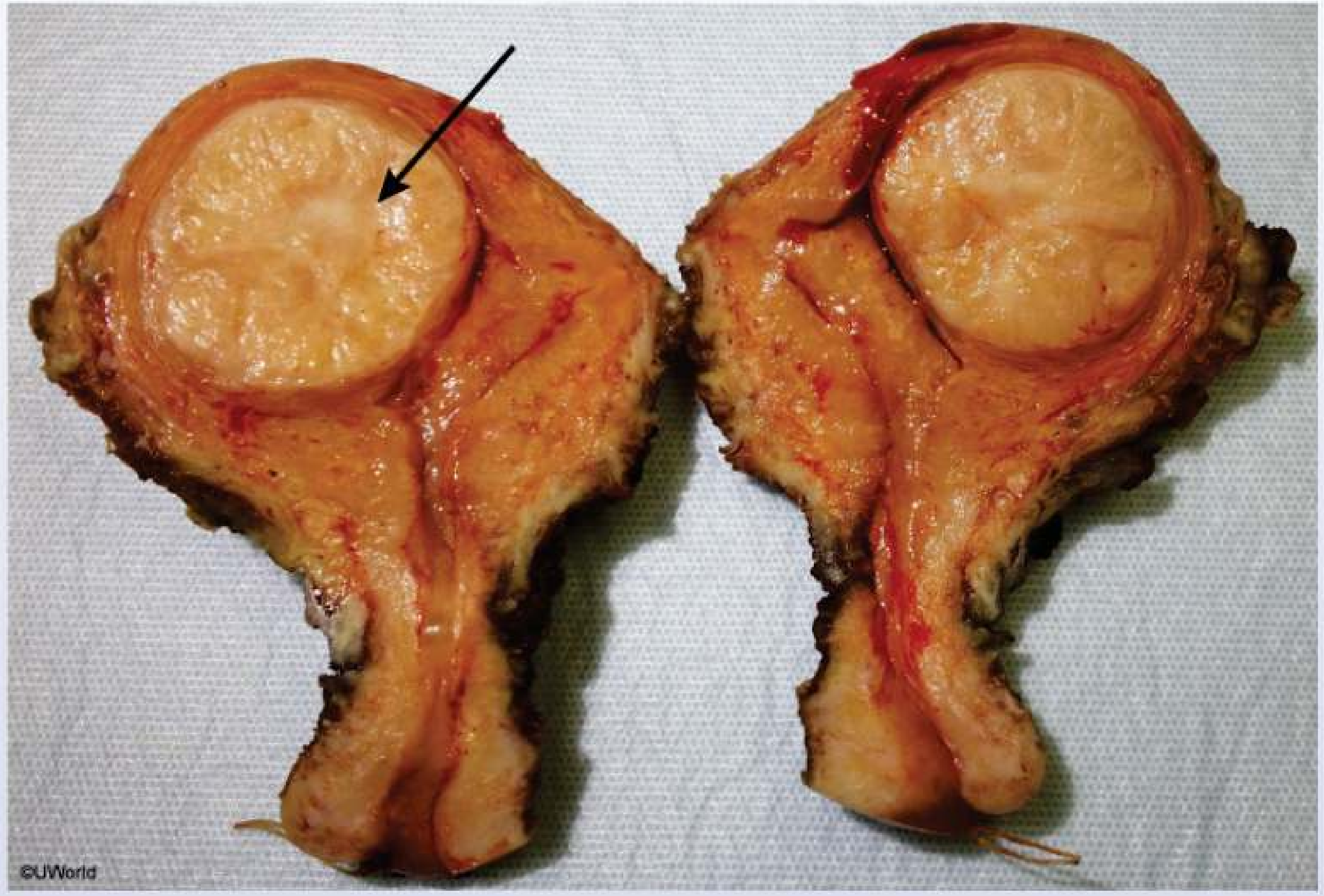
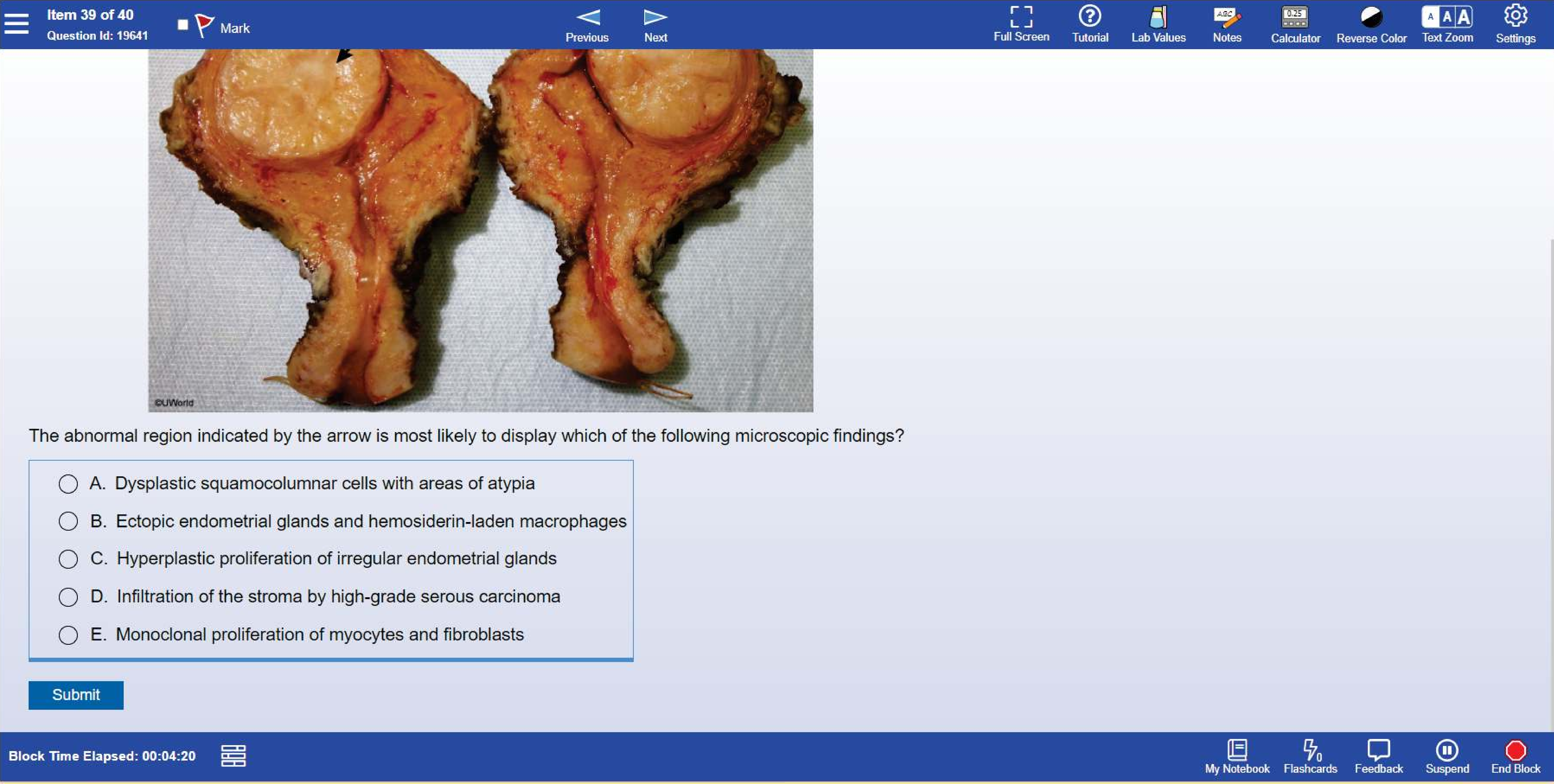
(Choice D) Progestin-only oral contraceptives decrease, not increase, the risk for ectopic pregnancy by

A 48-year-old woman comes to the office due to heavy menstrual bleeding for the last several months. The patient has monthly menses with 5-6 days of heavy bleeding and passage of large blood clots and increased abdominal cramping. She has no significant medical history and has had 2 vaginal deliveries. Her family history is significant for endometrial cancer in her mother. BMI is 24 kg/m^2. Vital signs are normal. Pelvic ultrasound shows a uterine mass. The patient undergoes a total abdominal hysterectomy; gross examination of the uterus is shown below:



The abnormal region indicated by the arrow is most likely to display which of the following microscopic findings?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The abnormal region indicated by the arrow is most likely to display which of the following microscopic findings?

- ○ A. Dysplastic squamocolumnar cells with areas of atypia
- ○ B. Ectopic endometrial glands and hemosiderin-laden macrophages
- ○ C. Hyperplastic proliferation of irregular endometrial glands
- ○ D. Infiltration of the stroma by high-grade serous carcinoma
- ○ E. Monoclonal proliferation of myocytes and fibroblasts

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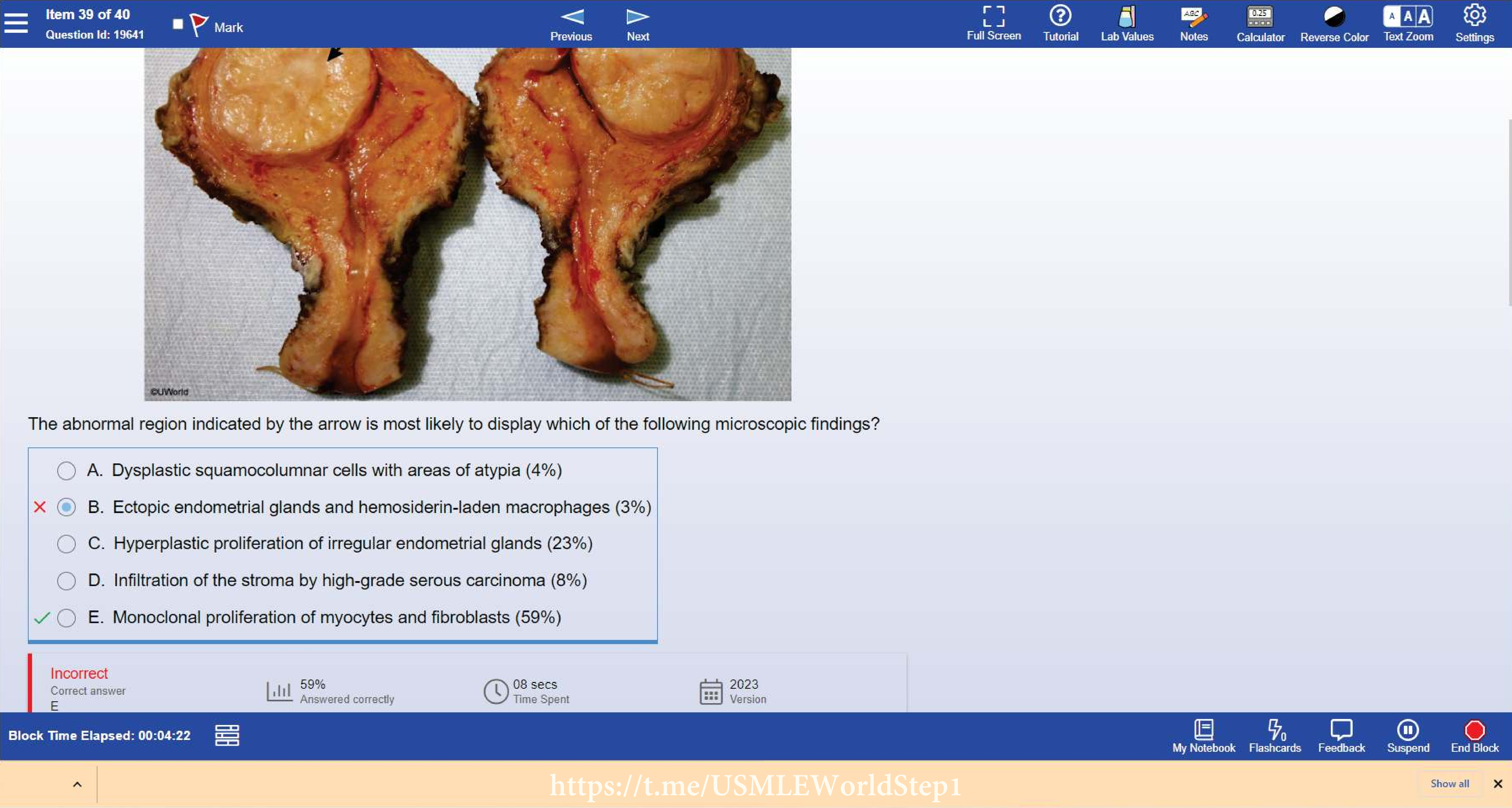
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The abnormal region indicated by the arrow is most likely to display which of the following microscopic findings?

○ A. Dysplastic squamocolumnar cells with areas of atypia (4%)

✗ ● B. Ectopic endometrial glands and hemosiderin-laden macrophages (3%)

○ C. Hyperplastic proliferation of irregular endometrial glands (23%)

○ D. Infiltration of the stroma by high-grade serous carcinoma (8%)

✓ ○ E. Monoclonal proliferation of myocytes and fibroblasts (59%)

Incorrect
Correct answer
E

59%
Answered correctly

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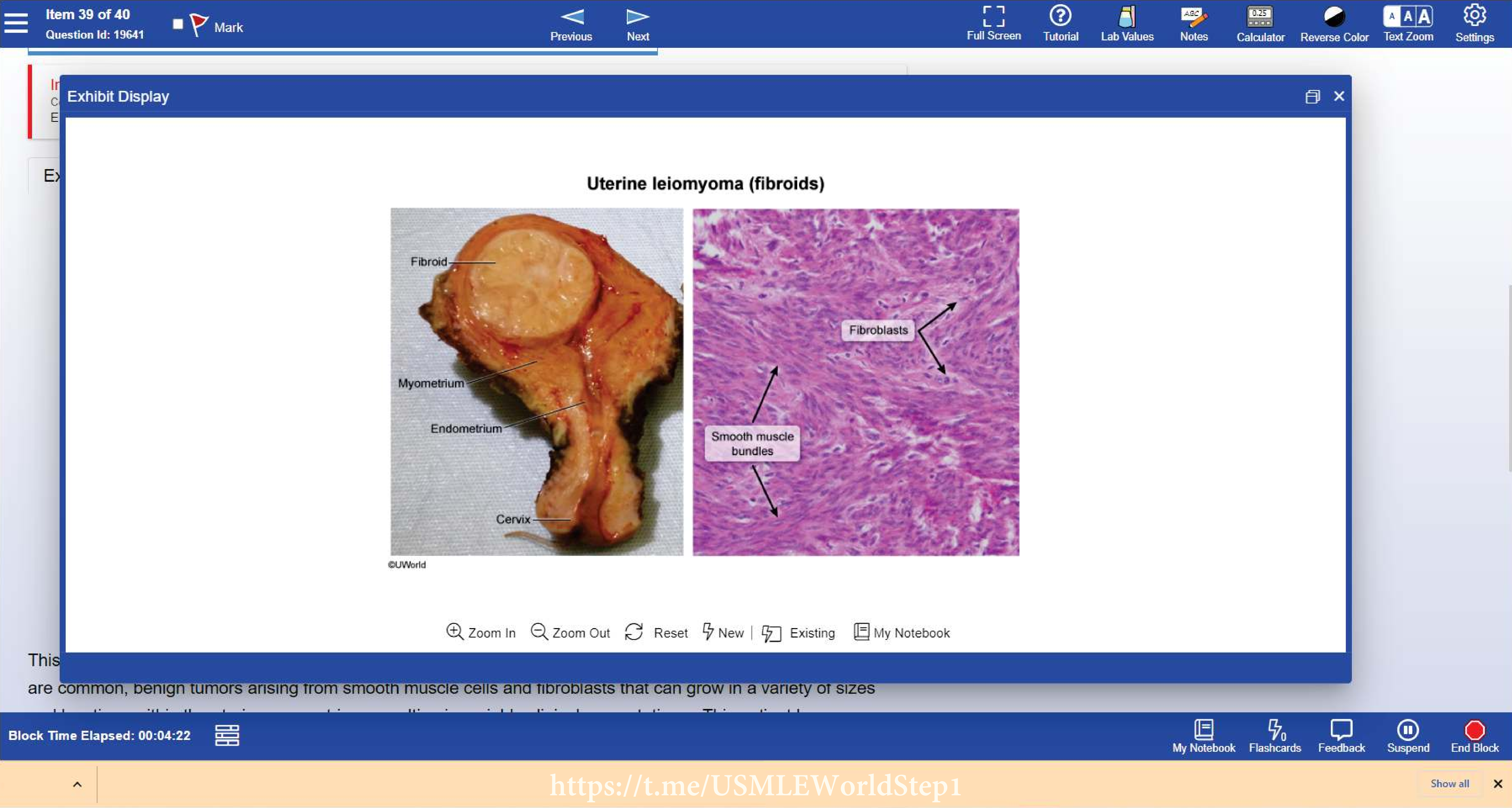
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Fibroid
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Cervix
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Uterine leiomyoma (fibroids)

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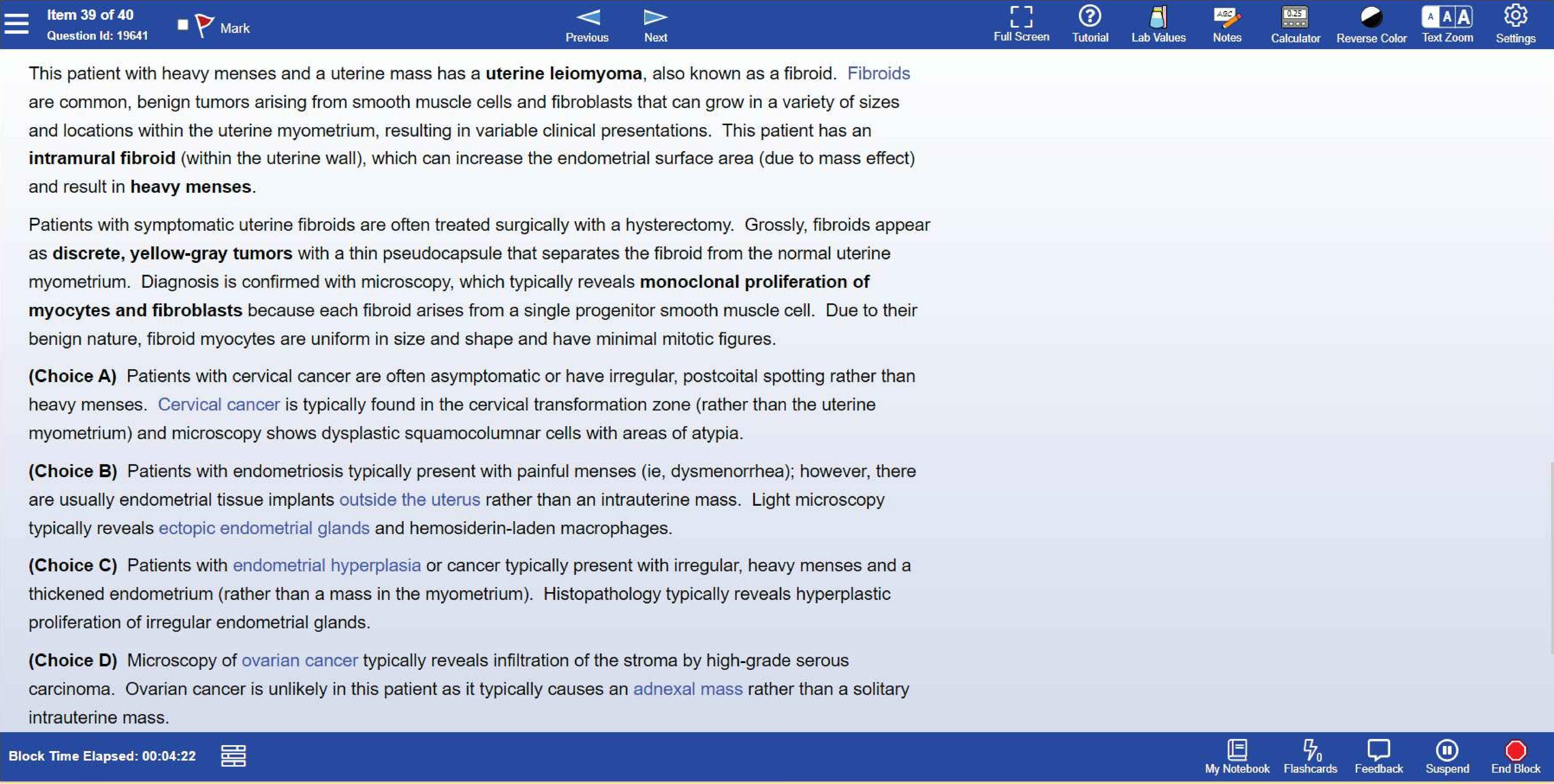
are common, benign tumors arising from smooth muscle cells and fibroblasts that can grow in a variety of sizes



This patient with heavy menses and a uterine mass has a **uterine leiomyoma**, also known as a fibroid. Fibroids are common, benign tumors arising from smooth muscle cells and fibroblasts that can grow in a variety of sizes and locations within the uterine myometrium, resulting in variable clinical presentations. This patient has an **intramural fibroid** (within the uterine wall), which can increase the endometrial surface area (due to mass effect) and result in **heavy menses**.

Patients with symptomatic uterine fibroids are often treated surgically with a hysterectomy. Grossly, fibroids appear as **discrete, yellow-gray tumors** with a thin pseudocapsule that separates the fibroid from the normal uterine myometrium. Diagnosis is confirmed with microscopy, which typically reveals **monoclonal proliferation of myocytes and fibroblasts** because each fibroid arises from a single progenitor smooth muscle cell. Due to their benign nature, fibroid myocytes are uniform in size and shape and have minimal mitotic figures.

(Choice A) Patients with cervical cancer are often asymptomatic or have irregular, postcoital spotting rather than heavy menses. Cervical cancer is typically found in the cervical transformation zone (rather than the uterine myometrium) and microscopy shows dysplastic squamocolumnar cells with areas of atypia.

(Choice B) Patients with endometriosis typically present with painful menses (ie, dysmenorrhea); however, there are usually endometrial tissue implants outside the uterus rather than an intrauterine mass. Light microscopy typically reveals ectopic endometrial glands and hemosiderin-laden macrophages.

(Choice C) Patients with endometrial hyperplasia or cancer typically present with irregular, heavy menses and a thickened endometrium (rather than a mass in the myometrium). Histopathology typically reveals hyperplastic proliferation of irregular endometrial glands.

(Choice D) Microscopy of ovarian cancer typically reveals infiltration of the stroma by high-grade serous carcinoma. Ovarian cancer is unlikely in this patient as it typically causes an adnexal mass rather than a solitary intrauterine mass.

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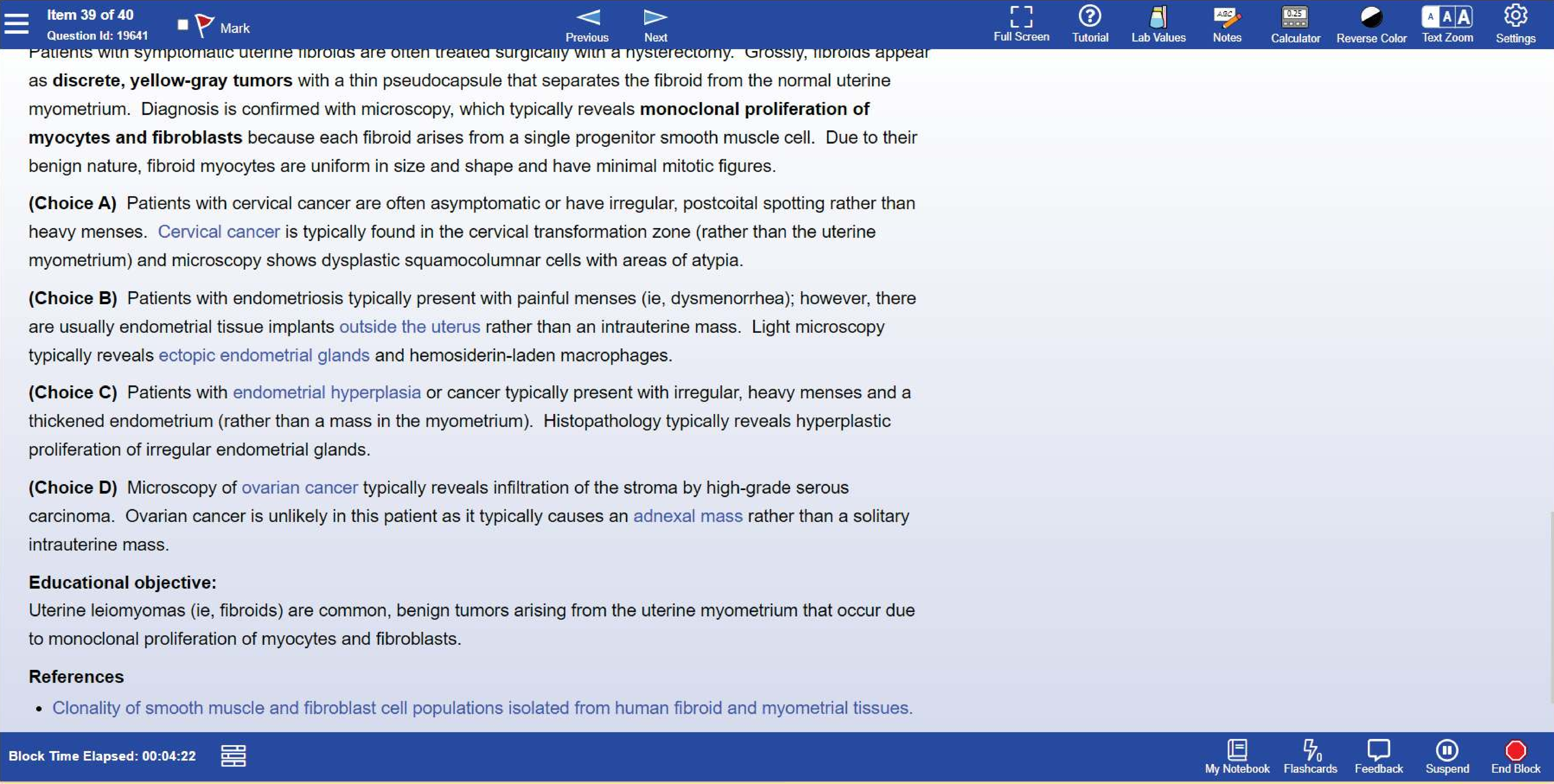

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(Choice C) Patients with endometrial hyperplasia or cancer typically present with irregular, heavy menses and a thickened endometrium (rather than a mass in the myometrium). Histopathology typically reveals hyperplastic proliferation of irregular endometrial glands.

(Choice D) Microscopy of ovarian cancer typically reveals infiltration of the stroma by high-grade serous carcinoma. Ovarian cancer is unlikely in this patient as it typically causes an adnexal mass rather than a solitary intrauterine mass.

Educational objective:

Uterine leiomyomas (ie, fibroids) are common, benign tumors arising from the uterine myometrium that occur due to monoclonal proliferation of myocytes and fibroblasts.

References

- Clonality of smooth muscle and fibroblast cell populations isolated from human fibroid and myometrial tissues.

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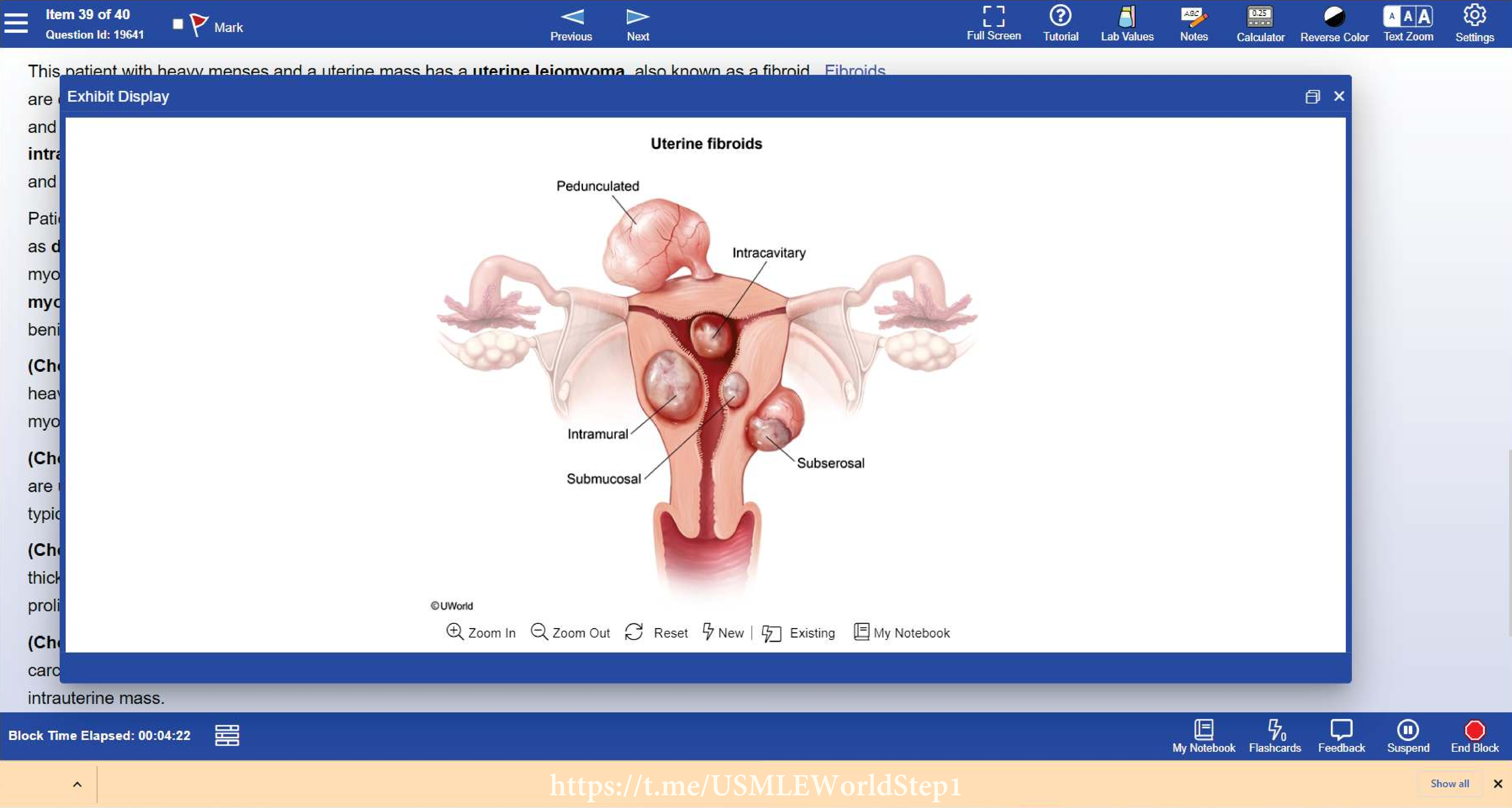
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This patient with heavy menses and a uterine mass has a **uterine leiomyoma**, also known as a fibroid. Fibroids

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Uterine fibroids

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This patient with heavy menses and a uterine mass has a **uterine leiomyoma**, also known as a fibroid. Fibroids

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Exhibit Display

Cervical squamous cell carcinoma

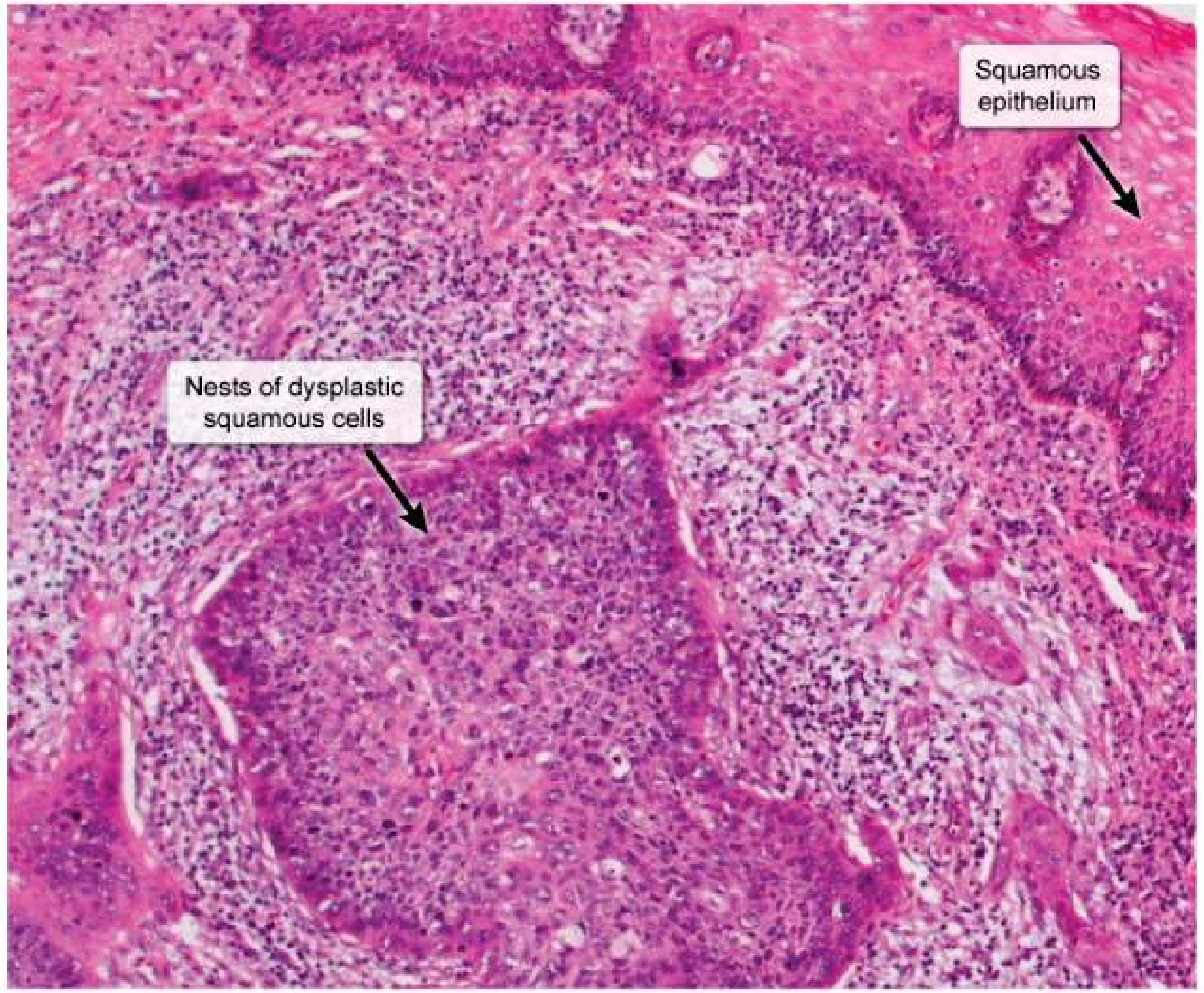
Squamous epithelium
Nests of dysplastic squamous cells

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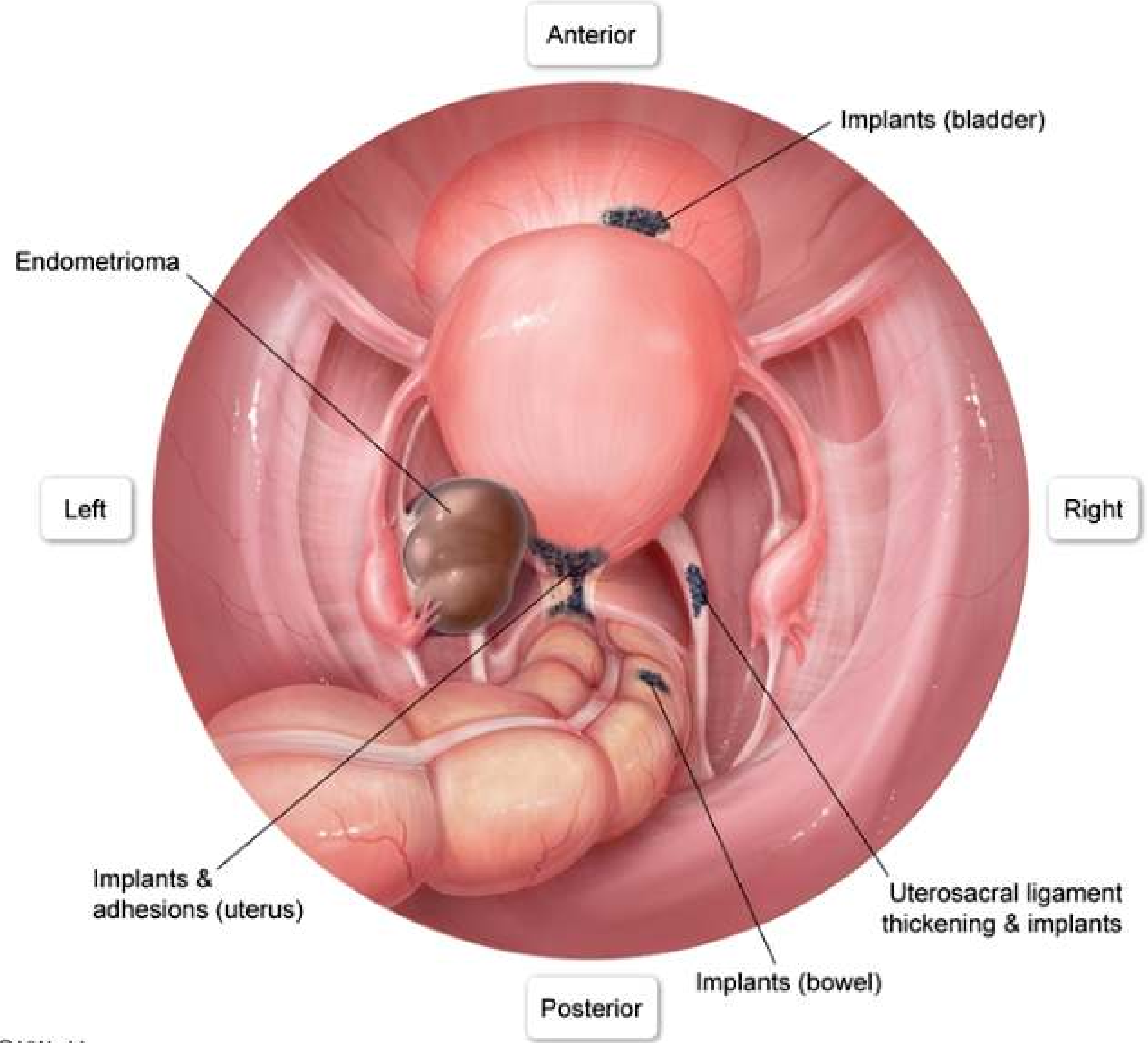
Exhibit Display

Pelvic endometriosis


Anterior
Implants (bladder)
Endometrioma
Left
Right
Implants &
adhesions (uterus)
Uterosacral ligament
thickening & implants
Implants (bowel)
Posterior

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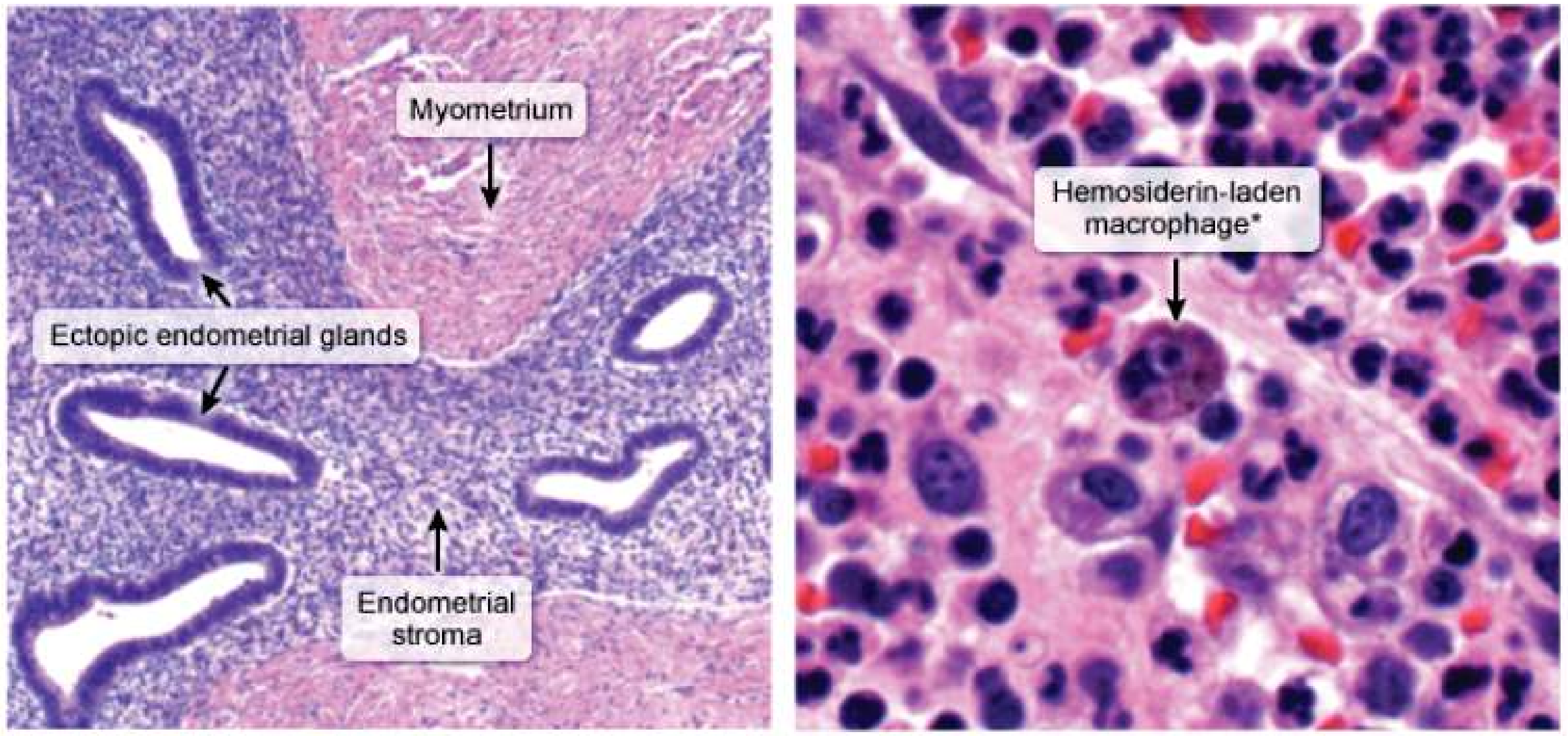
Endometriosis


Myometrium
Ectopic endometrial glands
Endometrial stroma
Hemosiderin-laden macrophage*

*Breakdown of red blood cells (chronic bleeding)

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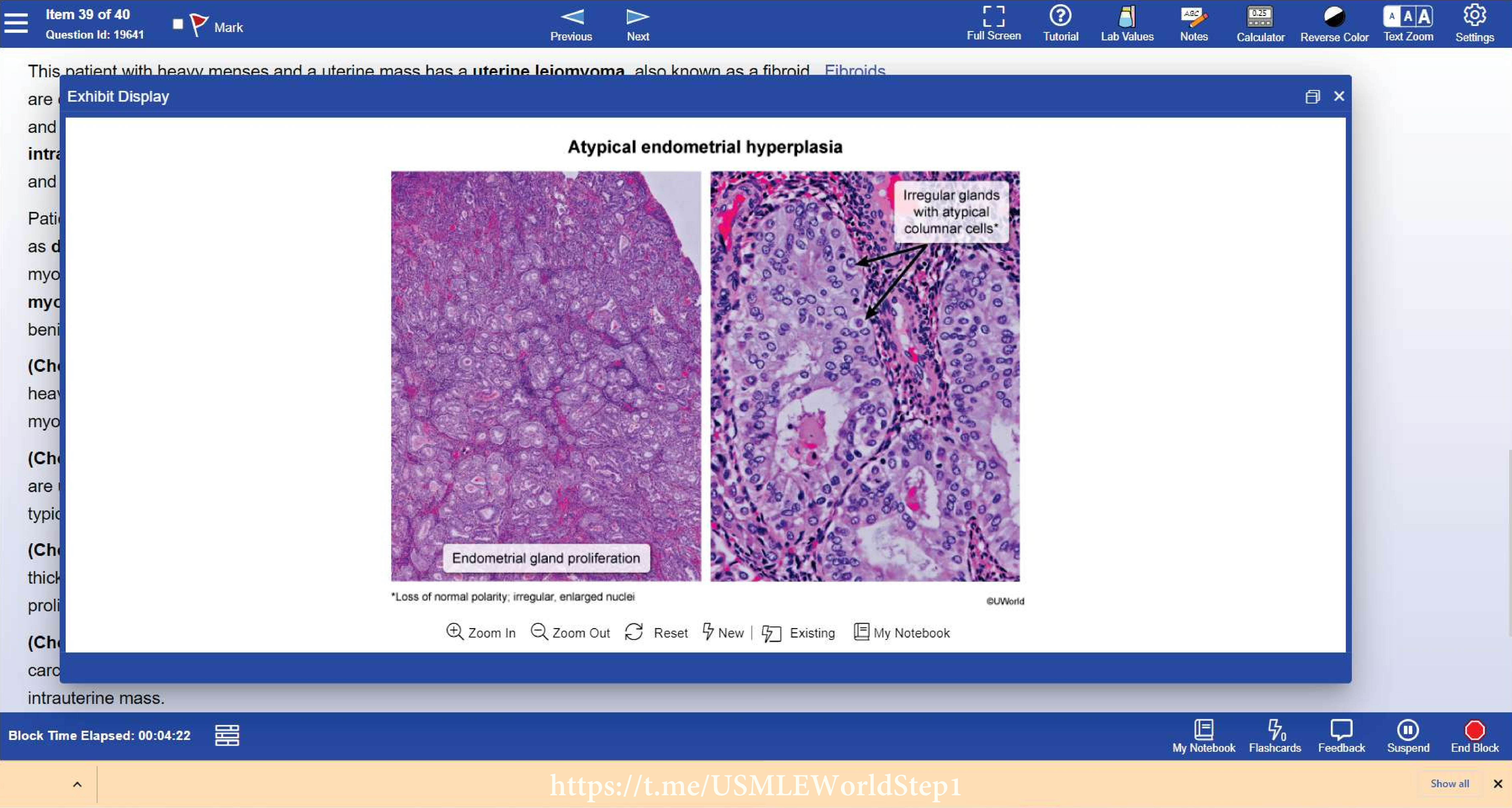
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This patient with heavy menses and a uterine mass has a **uterine leiomyoma**, also known as a fibroid. Fibroids

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Exhibit Display

Atypical endometrial hyperplasia

Endometrial gland proliferation
Irregular glands with atypical columnar cells*

*Loss of normal polarity; irregular, enlarged nuclei

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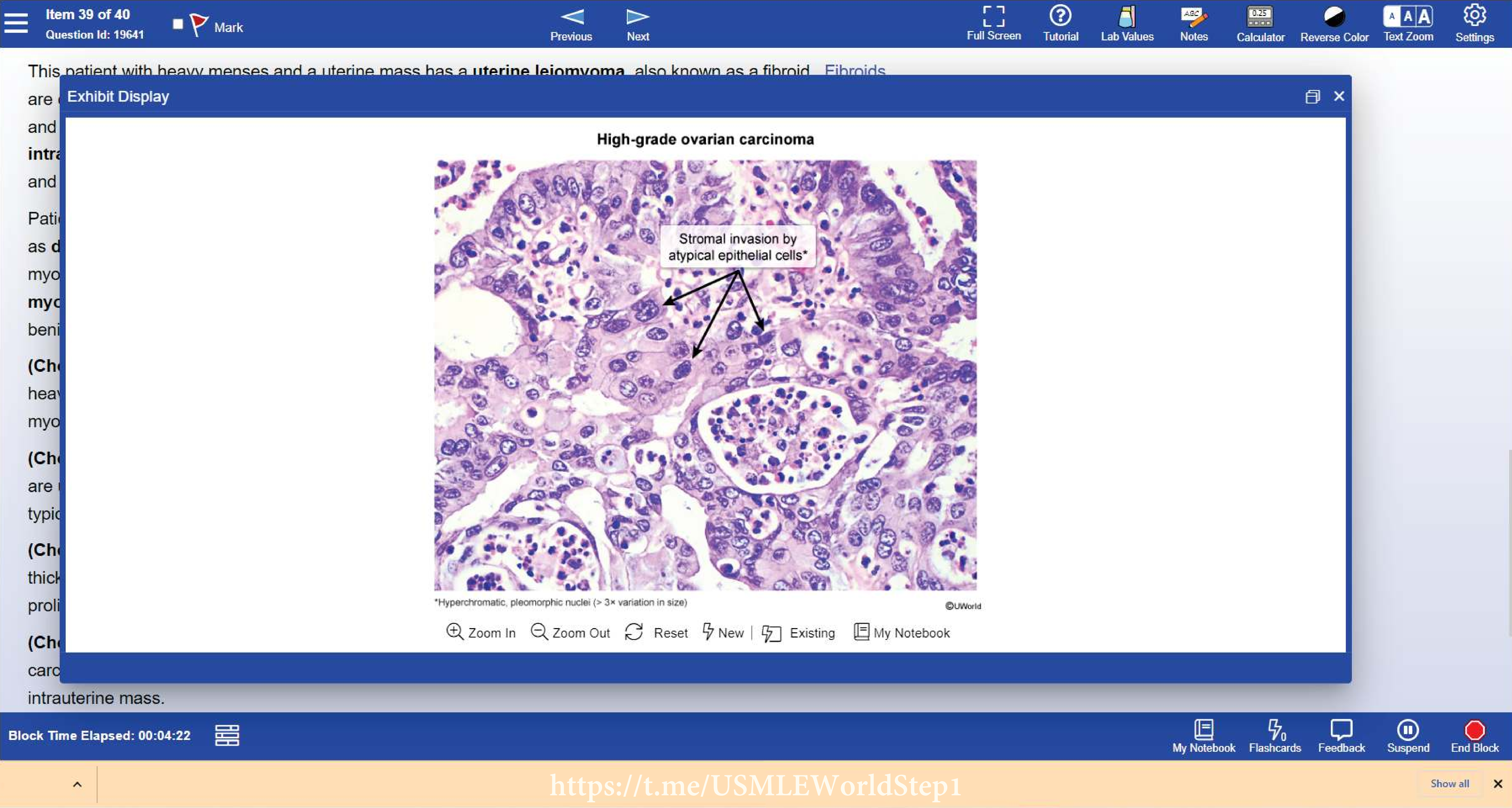

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intrauterine mass.

Exhibit Display

High-grade ovarian carcinoma

Stromal invasion by atypical epithelial cells*

*Hyperchromatic, pleomorphic nuclei (> 3× variation in size)

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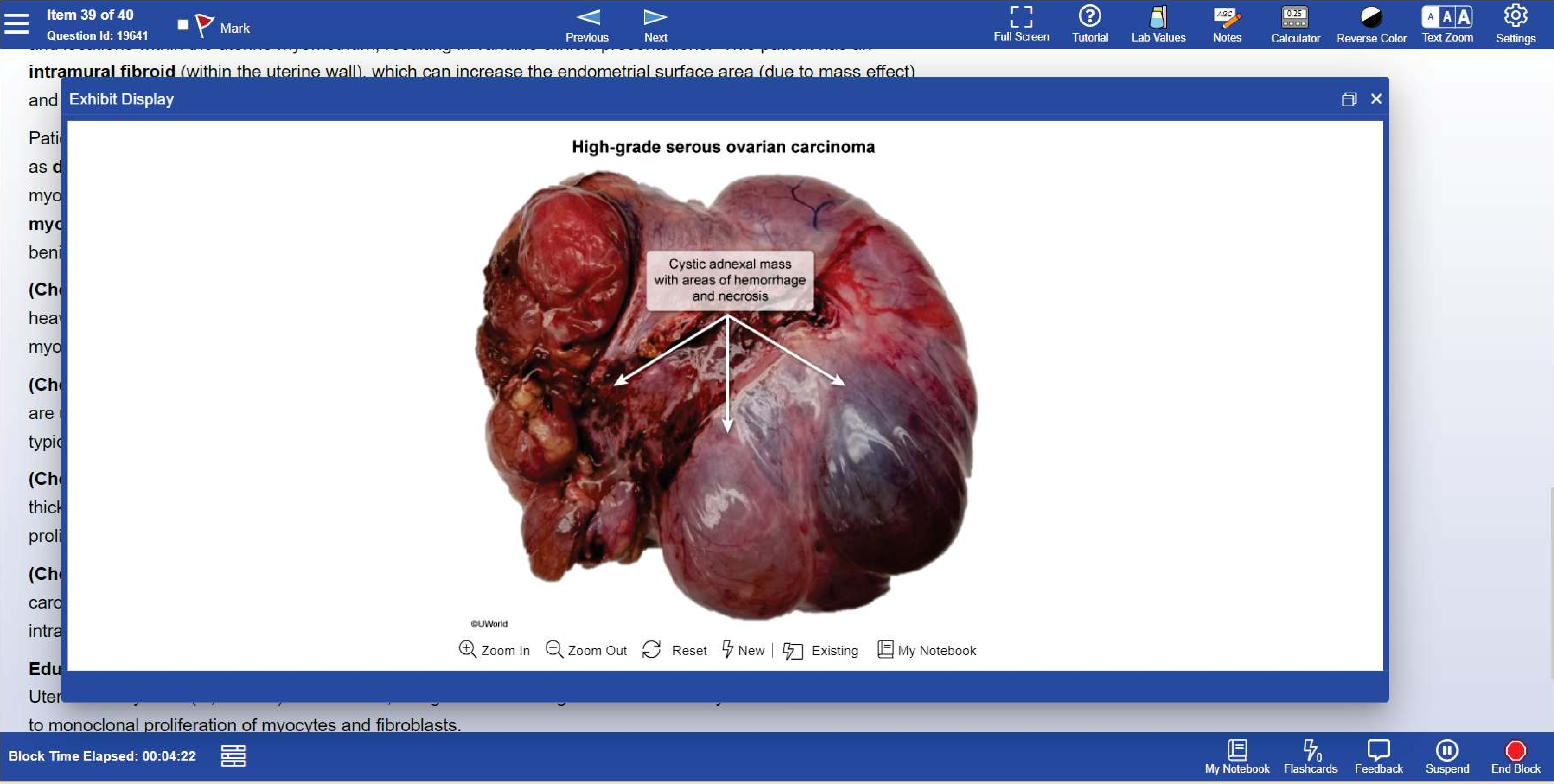
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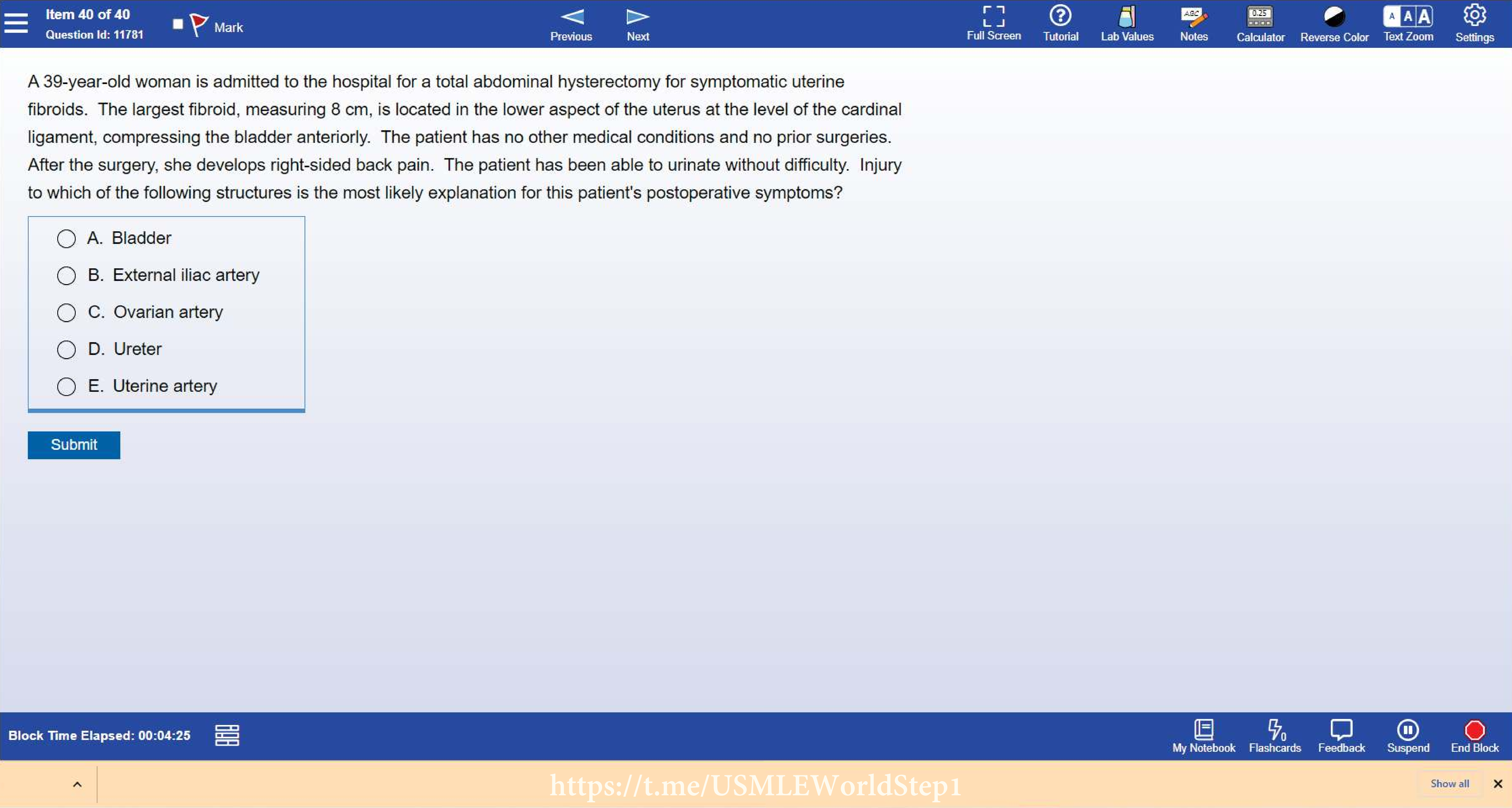
intramural fibroid (within the uterine wall), which can increase the endometrial surface area (due to mass effect)

High-grade serous ovarian carcinoma

Cystic adnexal mass with areas of hemorrhage and necrosis

to monoclonal proliferation of myocytes and fibroblasts.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A 39-year-old woman is admitted to the hospital for a total abdominal hysterectomy for symptomatic uterine fibroids. The largest fibroid, measuring 8 cm, is located in the lower aspect of the uterus at the level of the cardinal ligament, compressing the bladder anteriorly. The patient has no other medical conditions and no prior surgeries. After the surgery, she develops right-sided back pain. The patient has been able to urinate without difficulty. Injury to which of the following structures is the most likely explanation for this patient's postoperative symptoms?

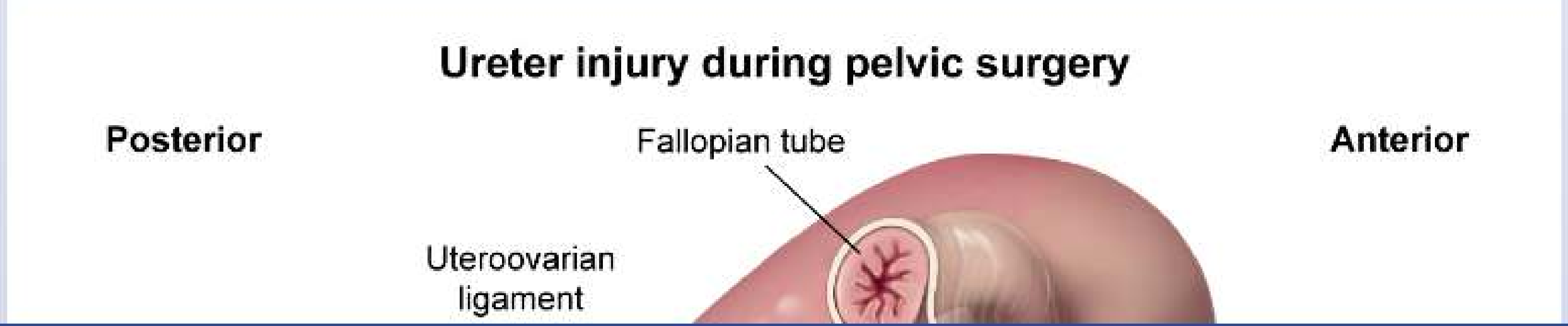
- ○ A. Bladder
- ○ B. External iliac artery
- ○ C. Ovarian artery
- ○ D. Ureter
- ○ E. Uterine artery

A 39-year-old woman is admitted to the hospital for a total abdominal hysterectomy for symptomatic uterine fibroids. The largest fibroid, measuring 8 cm, is located in the lower aspect of the uterus at the level of the cardinal ligament, compressing the bladder anteriorly. The patient has no other medical conditions and no prior surgeries. After the surgery, she develops right-sided back pain. The patient has been able to urinate without difficulty. Injury to which of the following structures is the most likely explanation for this patient's postoperative symptoms?

- ○ A. Bladder (2%)
- ✗ ● B. External iliac artery (8%)
- ○ C. Ovarian artery (14%)
- ✓ ○ D. Ureter (48%)
- ○ E. Uterine artery (26%)

Incorrect Correct answer D	48% Answered correctly	06 secs Time Spent	2023 Version

Explanation


Ureter injury during pelvic surgery

Show all

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D

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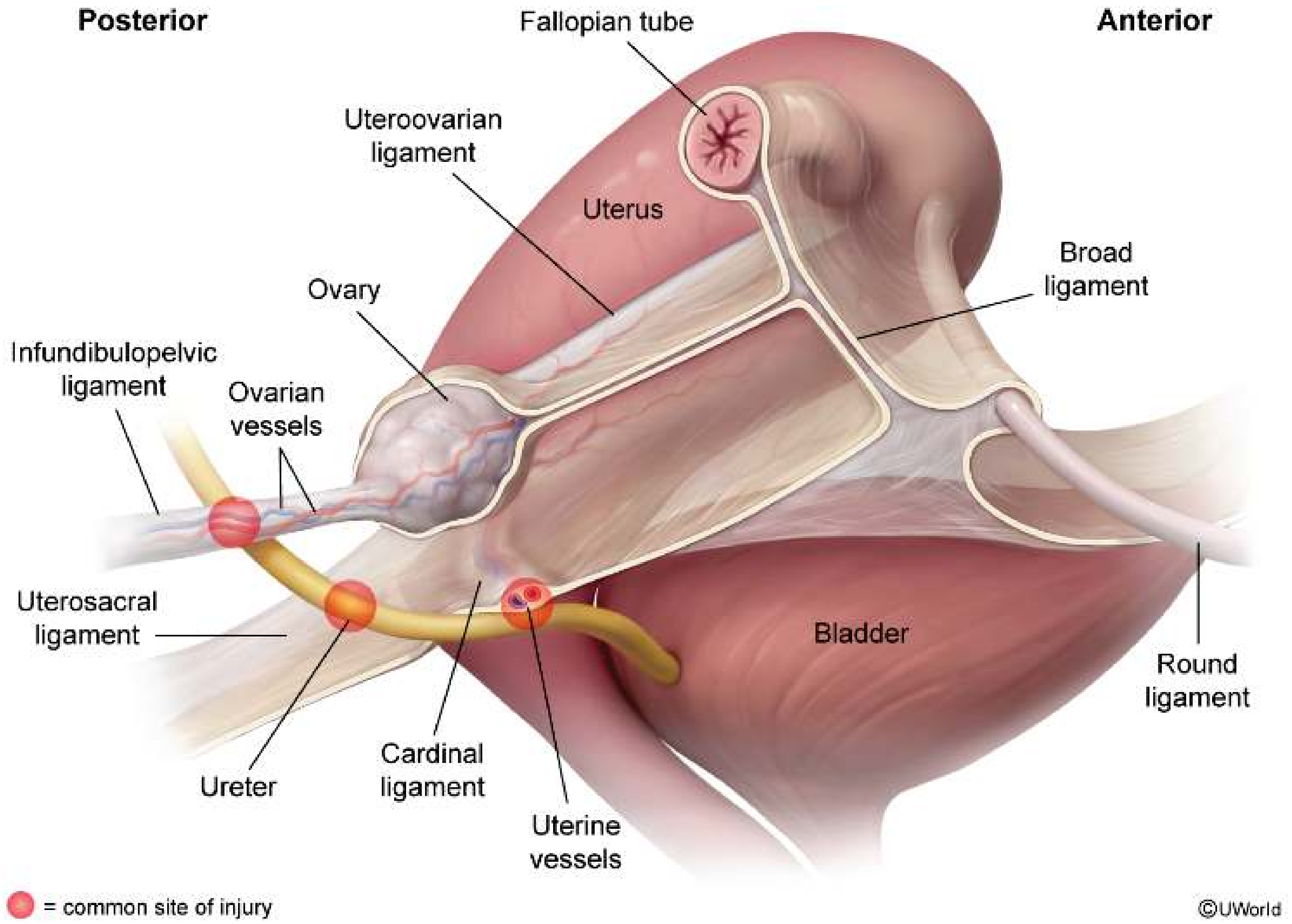
Ureter injury during pelvic surgery


Posterior
Anterior
Fallopian tube
Uteroovarian ligament
Uterus
Ovary
Broad ligament
Infundibulopelvic ligament
Ovarian vessels
Uterosacral ligament
Bladder
Round ligament
Cardinal ligament
Ureter
Uterine vessels
● = common site of injury

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This patient has a right **ureteral injury**, a potential complication of pelvic surgery (particularly hysterectomy) due to

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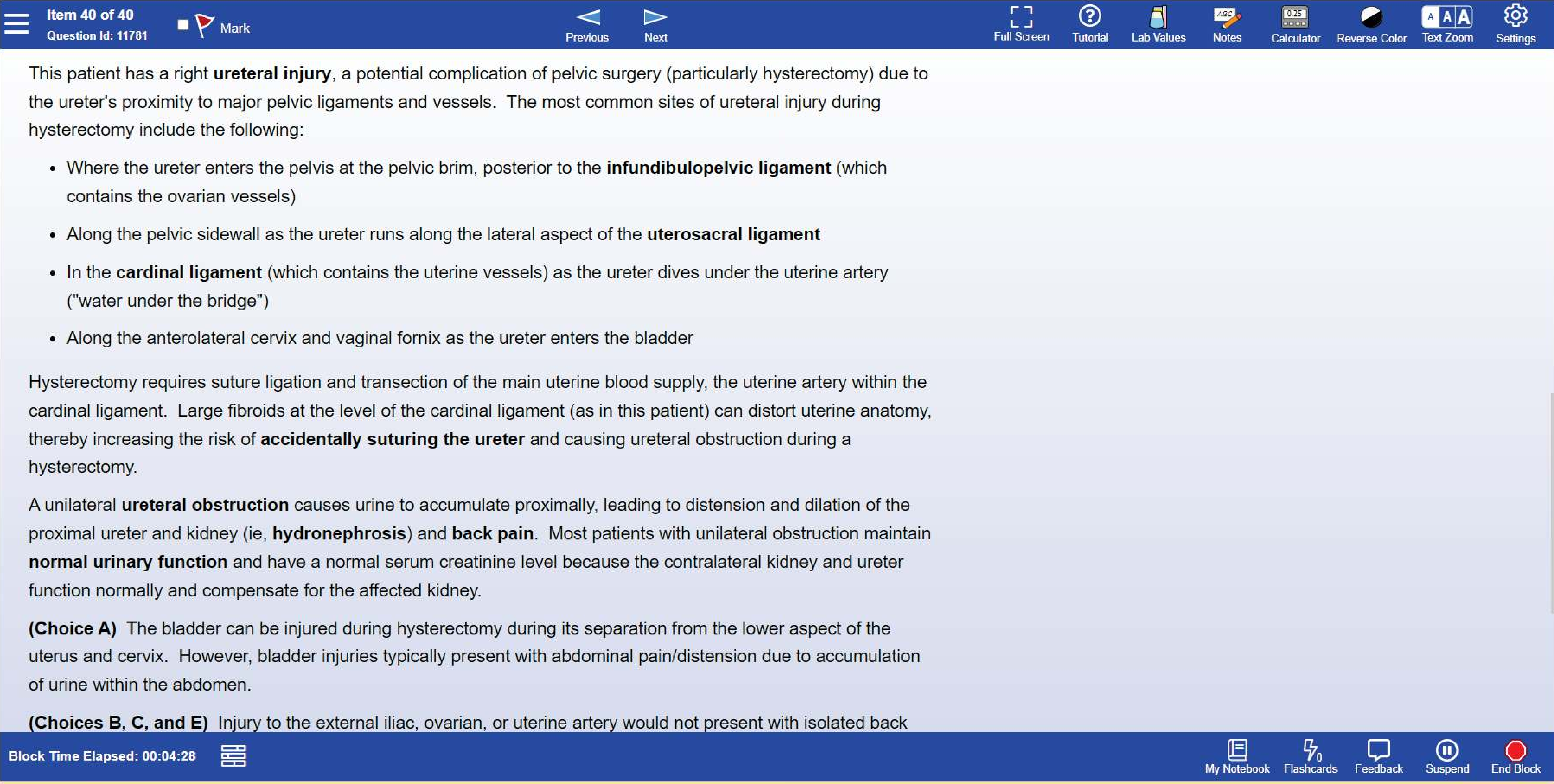
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This patient has a right **ureteral injury**, a potential complication of pelvic surgery (particularly hysterectomy) due to the ureter's proximity to major pelvic ligaments and vessels. The most common sites of ureteral injury during hysterectomy include the following:

- Where the ureter enters the pelvis at the pelvic brim, posterior to the **infundibulopelvic ligament** (which contains the ovarian vessels)
- Along the pelvic sidewall as the ureter runs along the lateral aspect of the **uterosacral ligament**
- In the **cardinal ligament** (which contains the uterine vessels) as the ureter dives under the uterine artery ("water under the bridge")
- Along the anterolateral cervix and vaginal fornix as the ureter enters the bladder

Hysterectomy requires suture ligation and transection of the main uterine blood supply, the uterine artery within the cardinal ligament. Large fibroids at the level of the cardinal ligament (as in this patient) can distort uterine anatomy, thereby increasing the risk of **accidentally suturing the ureter** and causing ureteral obstruction during a hysterectomy.

A unilateral **ureteral obstruction** causes urine to accumulate proximally, leading to distension and dilation of the proximal ureter and kidney (ie, **hydronephrosis**) and **back pain**. Most patients with unilateral obstruction maintain **normal urinary function** and have a normal serum creatinine level because the contralateral kidney and ureter function normally and compensate for the affected kidney.

(Choice A) The bladder can be injured during hysterectomy during its separation from the lower aspect of the uterus and cervix. However, bladder injuries typically present with abdominal pain/distension due to accumulation of urine within the abdomen.

(Choices B, C, and E) Injury to the external iliac, ovarian, or uterine artery would not present with isolated back

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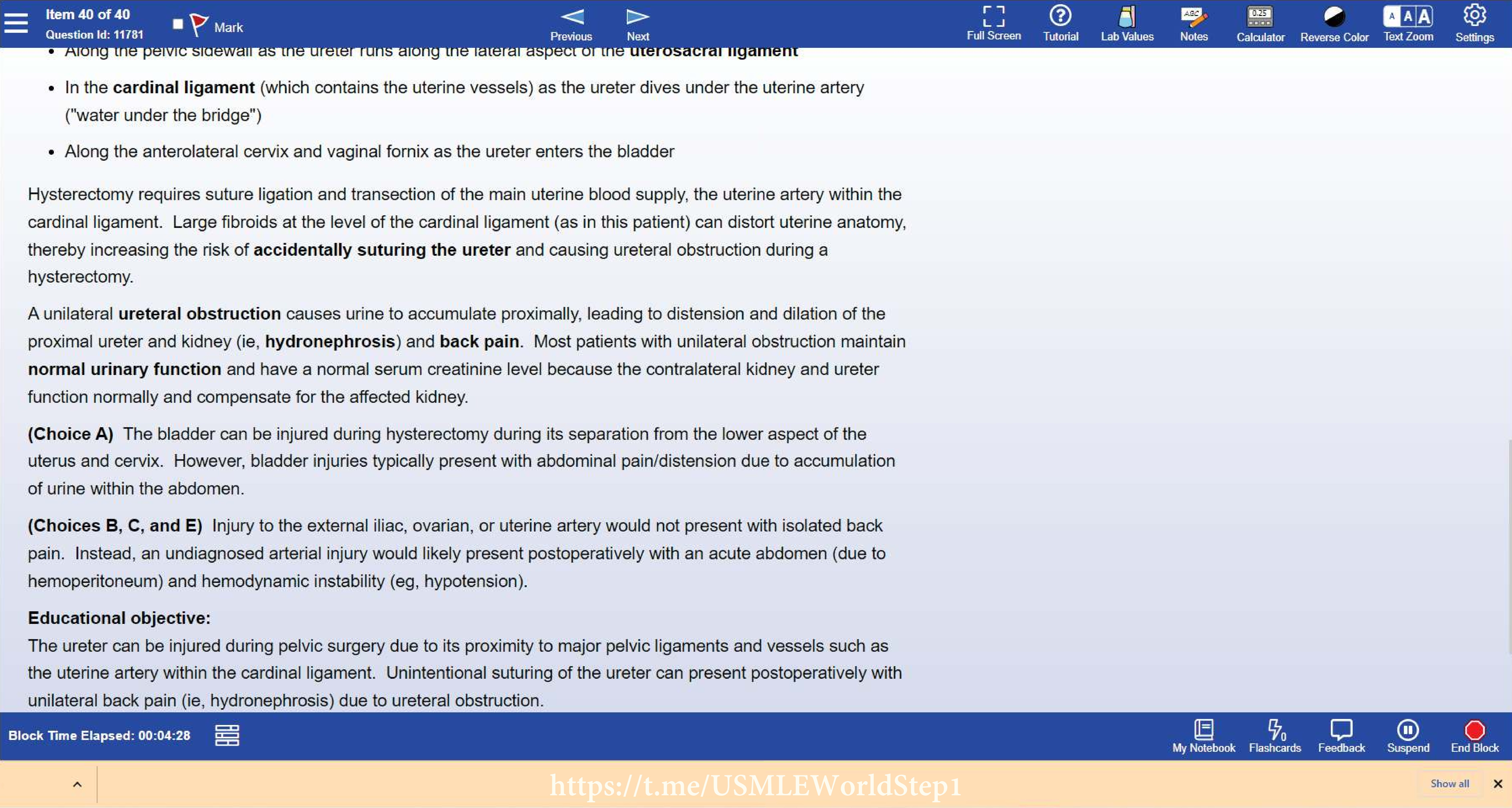
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(Choice A) The bladder can be injured during hysterectomy during its separation from the lower aspect of the uterus and cervix. However, bladder injuries typically present with abdominal pain/distension due to accumulation of urine within the abdomen.

(Choices B, C, and E) Injury to the external iliac, ovarian, or uterine artery would not present with isolated back pain. Instead, an undiagnosed arterial injury would likely present postoperatively with an acute abdomen (due to hemoperitoneum) and hemodynamic instability (eg, hypotension).

Educational objective:
The ureter can be injured during pelvic surgery due to its proximity to major pelvic ligaments and vessels such as the uterine artery within the cardinal ligament. Unintentional suturing of the ureter can present postoperatively with unilateral back pain (ie, hydronephrosis) due to ureteral obstruction.

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